Draft Comparative Effectiveness Review

Number xx

Treatments for Ankyloglossia and Ankyloglossia with Concomitant Lip-tie

Prepared for:
Agency for Healthcare Research and Quality
U.S. Department of Health and Human Services
540 Gaither Road
Rockville, MD 20850
www.ahrq.gov

Contract No.

Prepared by:

AHRQ Publication No. xx-EHCxxx
<Month Year>

This report is based on research conducted by an Evidence-based Practice Center (EPC) under contract to the Agency for Healthcare Research and Quality (AHRQ), Rockville, MD (Contract No. xxx-xxxx-xxxxx). The findings and conclusions in this document are those of the authors, who are responsible for its contents; the findings and conclusions do not necessarily represent the views of AHRQ. Therefore, no statement in this report should be construed as an official position of AHRQ or of the U.S. Department of Health and Human Services.

The information in this report is intended to help health care decisionmakers—patients and clinicians, health system leaders, and policymakers, among others—make well informed decisions and thereby improve the quality of health care services. This report is not intended to be a substitute for the application of clinical judgment. Anyone who makes decisions concerning the provision of clinical care should consider this report in the same way as any medical reference and in conjunction with all other pertinent information, i.e., in the context of available resources and circumstances presented by individual patients.

This report may be used, in whole or in part, as the basis for development of clinical practice guidelines and other quality enhancement tools, or as a basis for reimbursement and coverage policies. AHRQ or U.S. Department of Health and Human Services endorsement of such derivative products may not be stated or implied.

This report may periodically be assessed for the urgency to update. If an assessment is done, the resulting surveillance report describing the methodology and findings will be found on the Effective Health Care Program Web site at www.effectivehealthcare.ahrq.gov. Search on the title of the report.

Persons using assistive technology may not be able to fully access information in this report. For assistance contact EffectiveHealthCare@ahrq.hhs.gov

None of the investigators have any affiliations or financial involvement that conflicts with the material presented in this report.

Suggested citation: <Authors>. <Topic in Title Caps>. <Report Series Name in Title Caps No.> <#>. (Prepared by the <EPC Name> Evidence-based Practice Center under Contract No. <##>.) AHRQ Publication No. XX-EHCXXX-EF. Rockville, MD: Agency for Healthcare Research and Quality. <Month Year>. www.effectivehealthcare.ahrq.gov/reports/final.cfm.

Preface

The Agency for Healthcare Research and Quality (AHRQ), through its Evidence-based Practice Centers (EPCs), sponsors the development of systematic reviews to assist public- and private-sector organizations in their efforts to improve the quality of health care in the United States. These reviews provide comprehensive, science-based information on common, costly medical conditions, and new health care technologies and strategies.

Systematic reviews are the building blocks underlying evidence-based practice; they focus attention on the strength and limits of evidence from research studies about the effectiveness and safety of a clinical intervention. In the context of developing recommendations for practice, systematic reviews can help clarify whether assertions about the value of the intervention are based on strong evidence from clinical studies. For more information about AHRQ EPC systematic reviews, see www.effectivehealthcare.ahrq.gov/reference/purpose.cfm

AHRQ expects that these systematic reviews will be helpful to health plans, providers, purchasers, government programs, and the health care system as a whole. Transparency and stakeholder input are essential to the Effective Health Care Program. Please visit the Web site (www.effectivehealthcare.ahrq.gov) to see draft research questions and reports or to join an e-mail list to learn about new program products and opportunities for input.

We welcome comments on this systematic review. They may be sent by mail to the Task Order Officer named below at: Agency for Healthcare Research and Quality, 540 Gaither Road, Rockville, MD 20850, or by email to epc@ahrq.hhs.gov.

Richard G. Kronick, Ph.D.
Director
Agency for Healthcare Research and Quality

Yen-Pin Chiang, Ph.D.
Acting Deputy Director, Center for Evidence and Practice Improvement
Agency for Healthcare Research and Quality

Stephanie Chang, M.D., M.P.H.
Director, EPC Program
Center for Evidence and Practice Improvement
Agency for Healthcare Research and Quality

Kim M. Wittenberg, M.A.
Task Order Officer
Center for Evidence and Practice Improvement
Agency for Healthcare Research and Quality

.

Acknowledgments

<To be added>

Key Informants

In designing the study questions, the EPC consulted several Key Informants who represent the end-users of research. The EPC sought the Key Informant input on the priority areas for research and synthesis. Key Informants are not involved in the analysis of the evidence or the writing of the report. Therefore, in the end, study questions, design, methodological approaches, and/or conclusions do not necessarily represent the views of individual Key Informants.

Key Informants must disclose any financial conflicts of interest greater than $10,000 and any other relevant business or professional conflicts of interest. Because of their role as end-users, individuals with potential conflicts may be retained. The TOO and the EPC work to balance, manage, or mitigate any conflicts of interest.

The list of Key Informants who participated in developing this report follows:

<To be added>

Technical Expert Panel

In designing the study questions and methodology at the outset of this report, the EPC consulted several technical and content experts. Broad expertise and perspectives were sought. Divergent and conflicting opinions are common and perceived as healthy scientific discourse that results in a thoughtful, relevant systematic review. Therefore, in the end, study questions, design, methodologic approaches, and/or conclusions do not necessarily represent the views of individual technical and content experts.

Technical Experts must disclose any financial conflicts of interest greater than $10,000 and any other relevant business or professional conflicts of interest. Because of their unique clinical or content expertise, individuals with potential conflicts may be retained. The TOO and the EPC work to balance, manage, or mitigate any potential conflicts of interest identified.
The list of Technical Experts who participated in developing this report follows:

<To be added>

Peer Reviewers

Prior to publication of the final evidence report, EPCs sought input from independent Peer Reviewers without financial conflicts of interest. However, the conclusions and synthesis of the scientific literature presented in this report does not necessarily represent the views of individual reviewers.

Peer Reviewers must disclose any financial conflicts of interest greater than $10,000 and any other relevant business or professional conflicts of interest. Because of their unique clinical or content expertise, individuals with potential non-financial conflicts may be retained. The TOO and the EPC work to balance, manage, or mitigate any potential non-financial conflicts of interest identified.

The list of Peer Reviewers follows:

<To be added>

Ankyloglossia

Structured Abstract

Objectives. We systematically the reviewed the literature on surgical and nonsurgical treatments for infants and children with ankyloglossia and ankyloglossia and concomitant lip-tie.

Data Sources. We searched MEDLINE (PubMed), PsycINFO, Cumulative Index of Nursing and Allied Health Literature (CINAHL®) and EMBASE (Excerpta Medica Database) as well as the reference lists of included studies and recent systematic reviews. We conducted the searches between September 2013 and May 2014.

Review Methods. We included studies of interventions for ankyloglossia published in English. Two investigators independently screened studies against predetermined inclusion criteria and independently rated the quality of included studies. We extracted data into evidence tables and summarized them qualitatively.

Results. We included 52 unique studies comprising six RCTs (three good, one fair, two poor quality), three cohort studies (all poor quality), 28 case series, 14 case reports, and one unpublished thesis. Most studies assessed the effects of frenotomy on breastfeeding-related outcomes. Four RCTs reported improvements in breastfeeding efficacy using either maternally reported or observer ratings, while two RCTs found no improvement with observer ratings. Although mothers consistently reported improved breastfeeding effectiveness after frenotomy, outcome measures were heterogeneous and short term. Future studies could provide additional data to confirm or change the measure of effectiveness; thus we consider the strength of the evidence (SOE; confidence in the estimate of effect) to be low at this time. Pain outcomes improved for mothers of frenotomized infants compared with control in one study of 6-day old infants but not in studies of infants a few weeks older. Given these inconsistencies and the small number of comparative studies and participants, the SOE is low for an immediate reduction in nipple pain. Three studies with significant limitations reported improvements in other feeding outcomes with frenotomy, and three poor quality studies reported some improvements in articulation but mixed results related to fluent speech. Three poor quality comparative studies noted some improvements in social concerns and gains in tongue mobility in treated participants. SOE for all of these outcomes is insufficient. SOE is moderate for minor and short-term bleeding following surgery and insufficient for other harms (reoperation, pain).

Conclusions. A small body of evidence suggests that frenotomy may be associated with improvements in breastfeeding as reported by mothers, and potentially in nipple pain, but with small, short-term studies, inconsistently conducted, SOE is generally low to insufficient. Research is lacking on nonsurgical interventions as well as on outcomes other than breastfeeding.

Contents

Executive Summary ES-1
Introduction 1
Background 1
Ankyloglossia 1
Treatment Strategies 2
Scope and Key Questions 4
Scope of the Review 4
Key Questions 4
Analytic Framework 6
Organization of This Evidence Report 7
Uses of This Evidence Report 7
Methods 9
Topic Refinement and Review Protocol 9
Literature Search Strategy 9
Search Strategy 9
Inclusion and Exclusion Criteria 10
Study Selection 11
Data Extraction 11
Data Synthesis 12
Quality (Risk of Bias) Assessment of Individual Studies 12
Determining Quality Ratings 13
Strength of the Body of Evidence 13
Applicability 14
Results 15
Results of Literature Searches 15
Description of Included Studies 15
Key Question 1. Benefits of Interventions to Improve Breastfeeding Outcomes 17
Key Points 17
Overview of the Literature 17
Detailed Analysis 18
Key Question 2a. Benefits of Treatments to Mitigate Feeding Sequelae 24
Key Points 24
Overview of the Literature 24
Detailed Analysis 25
Key Question 2b. Benefits of Treatments to Prevent Other Sequelae 26
Key Points 26
Overview of the Literature 27
Detailed Analysis 27
Key Question 3. Benefits of Treatments to Prevent Social Concerns 31
Key Points 31
Overview of the Literature 31
Detailed Analysis 31
Key Question 4. Benefits of Simultaneously Treating Ankyloglossia and Concomitant Lip-Tie 33

Key Question 5. Harms of Treatments for Ankyloglosisia or Ankyloglosisia and Concomitant Lip-tie 34
Key Points 34
Overview of the Literature 34
Detailed Analysis 34

Discussion 39
Key Findings and Strength of Evidence 39
Findings in Relationship to What is Already Known 44
Applicability 45
Implications for Clinical and Policy Decisionmaking 47
Limitations of the Comparative Effectiveness Review Process 48
Limitations of the Evidence Base 48
Research Gaps 48
Conclusions 49

References 51
Abbreviations and Acronyms 56

Tables

Table A. Inclusion and Exclusion Criteria ES-5
Table B. Strength of the Evidence for Studies of Surgical Approaches for Anykloglossia ES-11
Table 1. Nonsurgical Treatment Approaches 3
Table 2. Structured Assessments Used in Ankyloglossia Literature 2
Table 3. PICOTS 5
Table 4. Inclusion and Exclusion Criteria 11
Table 5. Strength of Evidence Grades and Definitions 14
Table 6. Overview of Comparative Studies Included 16
Table 7. Breastfeeding Effectiveness Following Surgical Procedures 21
Table 8. Breastfeeding-associated Pain Scores After Surgical Procedures 24
Table 9. Feeding Sequelae 26
Table 10. Comparative Studies with Speech Outcomes 28
Table 11. Comparison of Surgical Approaches 30
Table 12. Outcomes of Interventions for Social Concerns Related to Tongue Mobility 33
Table 13. Outcomes Reported in Unpublished Thesis 37
Table 14. Strength of the Evidence for Studies Addressing Surgical Approaches for Ankyloglossia and Breastfeeding Outcomes 40
Table 15. Strength of the Evidence for Studies Addressing Surgical Approaches and Feeding Outcomes 41
Table 16. Strength of the Evidence for Studies Addressing Surgical Approaches and Other Outcomes 42
Table 17. Strength of the Evidence for Studies Addressing Surgical Approaches Social Concerns Related to Tongue Mobility 43
Table 18. Strength of the Evidence for Studies Addressing Harms of Surgical Approaches 44

Figures

Figure A. Analytic Framework for Ankyloglossia in Neonates and Infants ES-3

Figure B. Analytic Framework for Ankyloglossia in Children Up to 18 Years of Age.....ES-4
Figure 1. Analytic Framework for Ankyloglossia in Neonates and Infants 6-7
Figure 3. Disposition of Articles Identified by the Search Strategy.....15

Appendixes

Appendix A. Search Strategies
Appendix B. Sample Abstract and Full Text Review Forms
Appendix C. List of Excluded Studies
Appendix D. Evidence Tables
Appendix E. Quality Screening Tools
Appendix F. Quality Scoring Results
Appendix G. Case Reports of Harms
Appendix H. Conference Proceedings
Appendix I. Applicability

Executive Summary

Introduction

Ankyloglossia is a congenital condition characterized by an abnormally short, thickened, or tight lingual frenulum that restricts mobility of the tongue.[1] It variably causes reduced tongue mobility and has been associated with functional limitations in breastfeeding, swallowing, articulation, orthodontic problems including malocclusion, open bite, and separation of lower incisors, mechanical problems related to oral clearance, and psychological stress. Reported rates range from 2.1 to 10.7 percent,[2] but definitive incidence and prevalence statistics are elusive due to an absence of a criterion standard or clinically practical diagnostic criteria.

Recognition of potential benefits of breastfeeding in recent years has resulted in a renewed interest in the functional sequelae of ankyloglossia. Of infants with anterior or posterior ankyloglossia, there is a reported 25 to 80 percent incidence of breastfeeding difficulties including failure to thrive, maternal nipple damage, maternal breast pain, poor milk supply, maternal breast engorgement, and refusing the breast.[2] Ineffective latch is hypothesized to underlie these problems. Mechanistically, infants with restrictive ankyloglossia cannot extend their tongues over the lower gum line to form a proper seal and therefore use their jaws to keep the breast in the mouth for breastfeeding. Adequate tongue mobility is required, and infants with ankyloglossia often cannot overcome their deficiency with conservative measures such as positioning and latching techniques, thereby requiring surgical correction.[2]

Nonetheless, consensus on ankyloglossia's role in breastfeeding difficulties is lacking. A minority of surveyed pediatricians (10%) and otolaryngologists (30%) believe it commonly affects feeding, while 69 percent of lactation consultants feel that it frequently causes breastfeeding problems.[3] Therefore, depending on the audience, enthusiasm for its treatment varies. Currently, the National Health Service (NHS) and the Canadian Paediatric Society (CPS) recommend treatment only if it interferes with breastfeeding.[4] A standard definition of "interference" with breastfeeding is not provided, leaving room for interpretation and variation in treatment thresholds. The absence of data on the natural history of untreated ankyloglossia further promulgates uncertainty. Some propose that a short frenulum elongates spontaneously due to progressive stretching and thinning of the frenulum with age and use.[1] However, there are no prospective longitudinal data on the congenitally short lingual frenulum. Without this information it is difficult to inform parents fully about the long-term implications of ankyloglossia, thereby complicating the decision making process. Most ankyloglossia research concentrates on the infant and breastfeeding issues, but concerns beyond infancy may include speech-related issues and social concerns related to limited tongue mobility.

Treatment Strategies

Ankyloglossia may be treated with surgical or nonsurgical approaches. Surgical modalities include frenotomy, frenulectomy, and frenuloplasty. These interventions involve clipping or cutting of the lingual frenulum, generally without sedation. Laser frenotomy or frenulotomy has also been described, and proponents argue that its use is more exact and provides better hemostasis than standard frenotomy or frenulotomy. Frenuloplasty, more technically involved than frenotomy or frenulotomy, generally refers to rearranging tissue or adding grafts after making incisions and closing the resultant wound in a specific pattern to lengthen the anterior

tongue. Frenuloplasty is most commonly performed under a general anesthetic and used in older infants and children or in more complex frenulum repairs.

Nonsurgical approaches include speech therapy and lactation interventions and observation to determine if intervention is warranted.

Scope and Key Questions

Scope of the Review

This systematic review provides a review of potential benefits of treatments (surgical and nonsurgical) as well as harms associated with those therapies in individuals with ankyloglossia and tight labial frenulum (lip-tie) concomitant with ankyloglossia. We sought information on outcomes related to breast and bottle-feeding and related to tongue tie in later life (e.g., orthodontic and dental issues, speech, self-esteem).

Key Questions

We have synthesized evidence in the published literature to address the following Key Questions (KQs):

KQ1. What are the benefits of various treatments in breastfeeding newborns and infants with ankyloglossia intended to improve breastfeeding outcomes? Surgical treatments include frenotomy (anterior and/or posterior), frenuloplasty (transverse to vertical frenuloplasty), laser frenulectomy/frenulotomy, and Z-plasty repair. Nonsurgical treatments include complementary and alternative medicine (CAM) therapies (e.g. craniosacral therapy), lactation intervention, physical/occupational therapy, oral motor therapy, and stretching exercises/therapy.

KQ2a. What are the benefits of various treatments in newborns, infants, and children with ankyloglossia intended to prevent, mitigate, or remedy attributable medium and longterm *feeding* sequelae including trouble bottle feeding, spilling and dribbling, difficulty moving food boluses in the mouth and deglutition?

KQ2b. What are the benefits of various treatments in infants and children with ankyloglossia intended to prevent, mitigate, or remedy attributable medium and longterm *other* sequelae including articulation disorders, poor oral hygiene, oral and oropharyngeal dysphagia, sleep disordered breathing, orthodontic issues including malocclusion, open bite due to reverse swallowing, lingual tipping of the lower central incisors, separation of upper central incisors, crowding, narrow palatal arch, and dental caries?

KQ3. What are the benefits of various treatments for ankyloglossia in children up to 18 years of age intended to prevent or address social concerns related to tongue mobility (i.e., speech, oral hygiene, excessive salivation, kissing, spitting while talking, and self-esteem)?

KQ4. What are the benefits of simultaneously treating ankyloglossia and concomitant tight labial frenulum (lip-tie) in infants and children up to age 18 intended to improve or remedy breastfeeding, articulation, orthodontic and dental, and other feeding outcomes? What are the relative benefits treating only ankyloglossia when tight labial frenulum (lip-tie) is also diagnosed?

KQ5. What are the harms of treatments for ankyloglossia or ankyloglossia with concomitant lip-tie in neonates, infants, and children up to age 18?

Analytic Framework

Figure A. depicts Key Questions 1, 4, and 5 within the context of the PICOTS described in the document. The figure examines surgical and nonsurgical treatments in neonates and infants to improve breastfeeding outcomes. Intermediate outcomes include maternal nipple pain, ability to latch and maintain latch, tongue mobility, and aerophagia. Final outcomes include duration of breastfeeding, failure to thrive, infant weight gain and oral and oropharyngeal dysphagia. Harms (KQ5) may occur at any point after the intervention is received.

Figure A. Analytic framework for ankyloglossia in neonates and infants

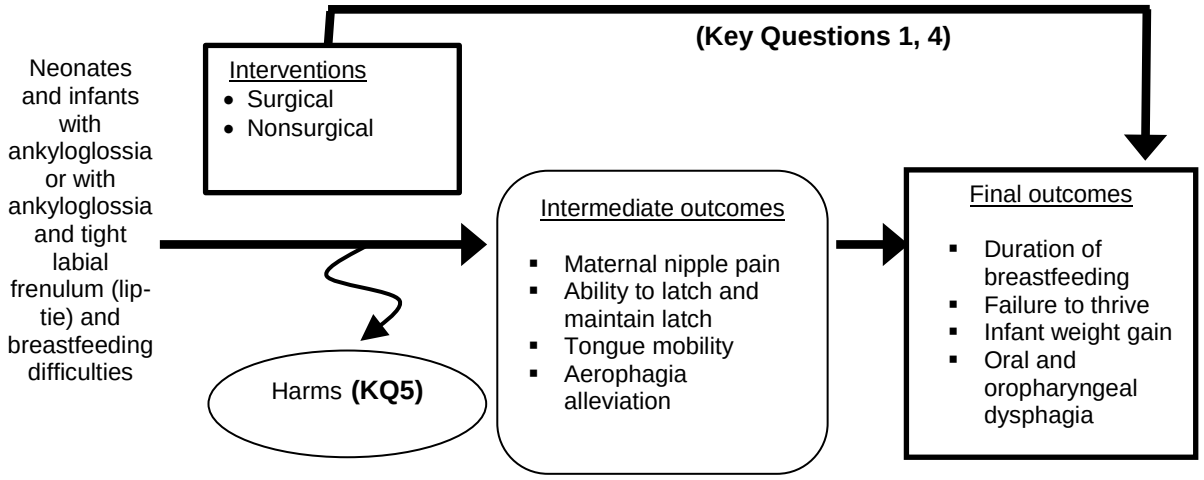
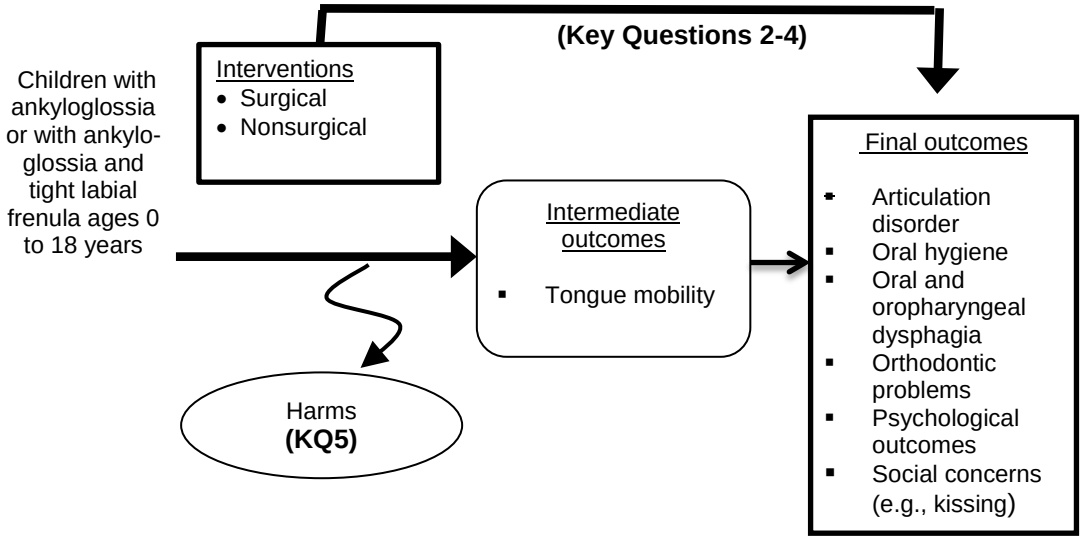


Figure B depicts Key Questions 2, 3, 4 and 5 within the context of the PICOTS described in the document. The figure examines surgical and nonsurgical treatments in infants and children with ankyloglossia (KQ2, KQ3) or ankyloglossia with concomitant tight labial frenulum (lip-tie) (KQ4). The intermediate outcome is tongue mobility and final health outcomes include articulation disorder, oral hygiene, oral and oropharyngeal dysphagia, orthodontic problems, psychological outcomes and social concerns including kissing. Harms (KQ5) may occur at any point after the intervention is received.

Figure B. Analytic framework for ankyloglossia in infants and children up to 18 years of age



Methods

Literature Search Strategy

A librarian employed search strategies provided in Appendix A of the full report to retrieve research on interventions for children with ankyloglossia. We searched MEDLINE® via the PubMed® interface, PsycINFO® (psychology and psychiatry literature), the Cumulative Index of Nursing and Allied Health Literature (CINAHL®) and EMBASE (Excerpta Medica Database). We limited searches to the English language and imposed no publication date restrictions. Our last search was conducted in May 2014. We manually searched reference lists of included studies and of recent narrative and systematic reviews and meta-analyses.

Inclusion and Exclusion Criteria

We developed criteria for inclusion and exclusion in consultation with a Technical Expert Panel (Table A).

Table A. Inclusion and exclusion criteria

Category	Criteria
Study population	Children ages 0-18 with ankyloglossia or ankyloglossia with concomitant tight labial frenulum (lip-tie); studies with participants with Van der Woude syndrome, Pierre Robin syndrome, Down syndrome, or craniofacial abnormalities were excluded as were studies of premature babies (<37 weeks of gestation[5])
Publication languages	English only
Admissible evidence (study design and other criteria)	Admissible designs RCTs, prospective and retrospective cohort studies, nonrandomized controlled trials, prospective and retrospective case series, and cross over studies Case reports to assess harms Other criteria Original research studies providing sufficient detail regarding methods and results to enable use and aggregation of the data and results Studies must address one or more of the following: • Surgical interventions (simple anterior frenectomy, laser frenulectomy, posterior frenulectomy, Z-plasty repair) • Nonsurgical treatments include complementary and alternative medicine (CAM) therapies (e.g. craniosacral therapy, myofascial release, and other chiropractic therapies), lactation intervention , speech therapy, physical therapy, oral motor therapy and stretching exercises/therapy • Baseline and outcome data (including harms) related to interventions for ankyloglossia Relevant outcomes must be able to be extracted from data in the papers Data must be presented in the aggregate (vs. individual participant data)

RCT=randomized controlled trial

Study Selection

Two reviewers independently assessed each abstract. If one reviewer concluded that the article could be eligible based on the abstract, we retained it for full-text assessment. Two reviewers independently assessed the full text of each included study. Disagreements were resolved by a senior reviewer.

Data Extraction and Synthesis

We extracted data from included studies into evidence tables that report study design, descriptions of the study populations (for applicability), description of the intervention, and baseline and outcome data on constructs of interest. Data were initially extracted by one team member and reviewed for accuracy by a second. The final evidence tables are presented in Appendix D of the full report.

We completed evidence tables for all included studies, and data are presented in summary tables and analyzed qualitatively in the text.

Quality (Risk of Bias) Assessment of Individual Studies

We used four tools to assess quality of individual studies: the Cochrane Risk of Bias Tool for Randomized Controlled Trials,[6] a cohort study assessment instrument based on questions and a tool for case series, both adapted from RTI Item Bank questions,[7] and a four-item harms

assessment instrument for cohort studies derived from the McMaster Quality Assessment Scale of Harms (McHarm) for Harms Outcomes[8] and the RTI Item Bank.[7] The tools are presented in Appendix E of the full report.

Quality assessment of each study was conducted by two team members independently. Discrepancies were adjudicated through discussion between the assessors to reach consensus or via a senior reviewer. The results of these tools were then translated to the AHRQ standard of "good," "fair," and "poor" quality designations as described in the full report. Quality ratings for each study are in Appendix F of the full report.

Strength of the Body of Evidence

Two senior investigators graded the entire body of evidence using methods based on the *Methods Guide for Effectiveness and Comparative Effectiveness Reviews.*[9] The team reviewed the final strength-of-evidence designation. Strength of the evidence is assessed for a limited set of critical outcomes, typically those related to effectiveness of an intervention and reported in comparative studies.

The possible grades were—

- High: High confidence that the evidence reflects the true effect. Further research is unlikely to change estimates.
- Moderate: Moderate confidence that the evidence reflects the true effect. Further research may change our confidence in the estimate of effect and may change the estimate.
- Low: Low confidence that the evidence reflects the true effect. Further research is likely to change confidence in the estimate of effect and is also likely to change the estimate.
- Insufficient: Evidence is either unavailable or does not permit a conclusion.

Applicability

We assessed applicability by identifying potential population, intervention, comparator, outcome, and setting (PICOS) factors likely to affect the generalizability of results (i.e., applicability to the general population of children with ankyloglossia). For this particular review, the most likely factors that could affect applicability are the severity/degree of ankyloglossia age range of participants, the setting of intervention (e.g., newborn nursery, outpatient office), and the provider (e.g., otolaryngologist, lactation consultant, dentist, pediatrician).

Results

Article Selection

We identified 1578 nonduplicative titles or abstracts with potential relevance, with 227 proceeding to full text review (Figure 3). We excluded 176 studies at full text review, which yielded 51 published studies included in the review. We also included one unpublished thesis in our results, thus the report summarizes data from 52 unique publications.

KQ 1. Benefits of Interventions Intended to Improve Breastfeeding Outcomes

Twenty-five studies addressed the benefits of surgical treatments intended to improve breastfeeding outcomes; there were no studies of nonsurgical treatments. These studies included

five randomized controlled trials conducted either in the United Kingdom (n=3),[10-12] United States (n=1),[13] or Israel (n=1)[14] and one poor quality retrospective cohort study conducted in the United States.[15] We rated the RCTs as good,[10, 11, 13] fair,[12] and poor[14] quality for outcomes related to breastfeeding effectiveness and maternal pain related to breastfeeding. One poor quality retrospective cohort study and 19 case series also addressed outcomes of surgical treatment. We focus on RCTs of higher quality in this summary but note that the lower quality studies typically reported improvements in breastfeeding effectiveness.

Two RCTs compared frenotomy to sham surgery,[11, 13] one to usual care,[10] one to intensive lactation consultation,[12] and one used a crossover design to compare frenotomy followed by sham surgery to sham surgery followed by frenotomy with assessment of breastfeeding after each order of intervention (i.e., frenotomy and sham).[14] Similarly, the retrospective cohort study compared frenotomy to usual care.[15]

Among the three RCTs that used a blinded independent reviewer to assess effectiveness,[10, 11, 13] one reported objective improvement in breastfeeding effectiveness based on the Infant Breastfeeding Assessment Tool (IBFAT; score range= 0 [poor feeding] to 12 [vigorous and effective feeding]) score immediately post-frenotomy compared with sham treatment (mean 11.6 ± 0.81 vs. 8.07 ± 0.86; p=0.026).[13] In contrast, in two of the three RCTs, the independent blinded observers did not detect a difference in breastfeeding improvement. Outcomes that failed to show a difference in these two RCTs included percent improvement (50% vs. 40%) immediately after intervention[11]and LATCH and IBFAT change 5-day post-intervention (LATCH change score: median 1 [IQR 0 – 2] vs. median 1 [IQR 0 – 2], p=0.52 and IBFAT change score: 0 [IQR -1.8 to 1.0] vs. 0 [IQR 0 – 1], p=0.36).[10]

Maternally reported outcomes differed from objective independent assessment. The earliest reported RCT used non-blinded maternally assessed breastfeeding effectiveness and reported that 96 percent of frenotomized infants had improved feeding within 48 hours compared with three percent in the control group, but this study had significant limitations.[12] In a later RCT, mothers again self-reported improved breastfeeding among infants immediately after frenotomy (78% in the treated group vs. 47% in the comparison group, p<0.02).[11]

One RCT reported significant and immediate improvement in maternally reported nipple pain among frenotomized infants compared with sham treatment.[13] Both remaining RCTs found nonsignificant reductions in maternally reported nipple pain between the frenotomy and sham groups at immediate[11] and 5-day[10]post-procedure assessments. However, in the one study that assessed pain at five days (the longest follow up), a large number of mothers in the control group crossed over to receive frenotomy before outcomes were assessed.[10].

Harms were rare and nonsignificant and are discussed in more detail below, in KQ5.

KQ 2a. Benefits of Treatments to Mitigate Feeding Sequelae

Three studies examined medium- and long-term benefits related to feeding outcomes and sequelae of various interventions for infants and children with ankyloglossia.[12, 16, 17] One was an RCT[12] (fair quality for feeding outcomes) and one was a poor quality retrospective cohort study[16]; the remaining study was a case series so provided no data for comparison.[17]

In one RCT that included bottle fed infants, 76 percent had major problems with dribbling, and 71 percent had “excess wind” (gas). Mothers reported significant improvement in bottle feeding in all eight infants who received the frenotomy and in none of the nine who did not. The interval to ascertainment of the outcomes was not specifically reported, but outcomes were obtained within the first 4 weeks of life.[12]

The retrospective cohort study compared parent-reported (typically maternal) outcomes at age 3 years for children born in 2010 who 1) received frenotomy for tongue-tie (n=71; frenotomy group), 2) were offered but declined frenotomy for tongue-tie (n=15; no frenotomy group), and 3) children without ankyloglossia (n=18; control group).[16] The frenotomy group performed better than the no frenotomy group at age 3 years on (a) cleaning the teeth with the tongue, (b) licking the outside of the lips, and (c) eating ice cream and did not differ significantly from the comparison group without ankyloglossia.

KQ 2b: Benefits of Treatments to Prevent Other Sequelae

Two cohort studies attempted to assess the effectiveness of frenotomy for preventing other sequelae,[16, 18] and one RCT compared two surgical approaches to frenotomy. [19] A speech language pathologist measured speech outcomes in two studies[18, 19] with the third using parental assessment.[16] No studies included data related to sleep disordered breathing, occlusal issues and dysphagia in the non-breastfeeding child.

Two poor quality cohort studies[16, 18] reported an improvement in articulation and intelligibility with ankyloglossia treatment, but benefits in word, sentence and fluent speech were unclear. The one poor quality RCT comparing surgical methods reported improved articulation in patients treated with four-flap-Z-frenuloplasty compared to horizontal-to-vertical frenuloplasty.[19] Numerous non-comparative studies [20-26]reported a speech benefit after treating ankyloglossia; however these studies primarily discussed modalities, with safety, feasibility or utility as the main outcome, rather than speech itself, and provide no comparative data.

KQ3: Benefits of Treatments to Prevent Social Concerns Related to Tongue Mobility

Only one poor quality retrospective cohort study assessed outcomes related to social concerns other than speech in 3 year old children who had received frenotomy as infants.[16] The group that had received frenotomy had better parent-reported ability to clean teeth with tongue, lick outside of lips, and eat ice cream compared with untreated participants.

KQ4: Benefits of Simultaneously Treating Ankyloglossia and Lip-Tie

We did not identify any studies addressing this question.

KQ5: What are the Harms of Treatments for Ankyloglossia or Ankyloglossia with Concomitant Lip-tie in Neonates, Infants and Children up to Age 18?

In order to identify all possible harms, we sought harms from all comparative studies and case series that we identified as potentially providing effectiveness data, and we sought case reports of harms. With this approach, we looked for harms in 45 studies that reported that they had looked for harms, either reporting actual harms or specifically indicating that they found none. These included six RCTs, one cohort study, 24 case series, and 14 case reports. Most studies that reported harms information explicitly noted that no significant harms were observed (n=18) or reported minimal harms. Among studies reporting harms, bleeding was most

frequently reported. Bleeding was typically described as minor and limited. Few studies described what specific methods they used to collect harms data.

Discussion

Key Findings

Most of the studies that met criteria for this review addressed outcomes related to breastfeeding. Overall, three good[10, 11, 13] and one fair[12] quality RCTs assessed whether surgical treatment of ankyloglossia improved breastfeeding effectiveness. While only one of three RCTs that used blinded independent observers found significantly improved breastfeeding effectiveness among frenotomized infants immediately post-procedure, [13] maternally reported breastfeeding effectiveness was significantly improved in the treated group compared to untreated in two of two RCTs that evaluated it either as a primary[12] or secondary[11] outcome. A third RCT evaluated the mother's breastfeeding self-efficacy and found a significant improvement from baseline in the frenotomy group 5-days post-procedure.[10] In all, there is some evidence that maternally reported breastfeeding outcomes improve. Data are unavailable to assess the durability of effects.

These same studies had disparate findings about whether frenotomy decreased maternal nipple pain during breastfeeding. Only the RCT performed on infants at 6 days of age showed a significant reduction in maternal pain.[13] Those performed on infants a few weeks older did not report either an immediate[11] or 5-day[10] reduction in pain. The difference between earlier frenotomy and later frenotomy on nipple pain may relate to cumulative trauma on the breast from several additional weeks with inefficient latch from tongue-tied infants.

We identified three studies examining feeding outcomes other than breastfeeding: one RCT,[12] one poor quality retrospective cohort study,[16] and one case series.[17] Bottle feeding and ability to use the tongue to eat ice cream and clean the mouth improved more in treatment groups in comparative studies. Supplementary bottle feedings decreased over time in the case series.

Following breastfeeding outcomes, outcomes related to speech were most often reported in the ankyloglossia literature. Two poor quality cohort studies[16, 18] reported an improvement in articulation and intelligibility with ankyloglossia treatment, but benefits in word, sentence and fluent speech were unclear. One poor quality RCT reported improved articulation in patients treated with Z-frenuloplasty compared with horizontal-to-vertical frenuloplasty.[19] Numerous non-comparative studies reported a speech benefit after treating ankyloglossia; however these studies primarily discussed modalities, with safety, feasibility or utility as the main outcome, rather than speech itself.[23, 26-28]

Few studies addressed social concerns. One retrospective cohort study noted improvements in using the tongue to clean the teeth and for licking in the treatment group compared with untreated participants.[16] In two comparative studies reporting on tongue mobility, mobility improved in treated patients.[18, 19]

Harms of surgical interventions included bleeding, which was typically self-limiting, and need for re-operation, which was rare. Eighteen studies reported that no significant harms were observed.

Strength of Evidence

Breastfeeding Outcomes

Few comparative studies of higher quality have addressed the effectiveness of surgical interventions to improve breastfeeding outcomes. Mothers consistently reported improved breastfeeding effectiveness, but outcome measures were heterogeneous and very short term. Future studies could provide additional data to confirm or change the measure of effectiveness; thus we consider the SOE to be low at this time. We considered the strength of the evidence (confidence in the estimate of effect) to be low for an immediate reduction in nipple pain. Improvements were reported in the current studies, but additional studies are needed to confirm and support these results. Only one poor quality cohort study addressed effects on the length of breastfeeding; thus, we considered the strength of the evidence to be insufficient.

Other Feeding Outcomes

With only two comparative studies, both with significant study limitations, existing data are insufficient to draw conclusions about the benefits and harms of surgical interventions for infants and children with ankyloglossia on medium- and long-term feeding outcomes. The studies used different populations and measured different outcomes.

Speech Outcomes

Given the lack of good quality studies and limitations in the measurement of outcomes, we considered the strength of the evidence for the effect of surgical interventions to improve speech and articulation to be insufficient.

Social Concerns Related to Tongue Mobility

With only one poor quality comparative study, strength of the evidence related to the ability of treatment for ankyloglossia to alleviate social concerns is currently insufficient. Also, with only three comparative studies with small sizes and limitations in the measurement of outcomes related to tongue mobility, we considered the strength of the evidence for the effect of surgical interventions to improve the short-term outcome of mobility to be insufficient.

Harms

We considered the strength of the evidence for minimal and short-lived bleeding as a harm of surgical interventions as moderate based on an expanded search for harms reports in addition to the comparative data We considered the strength of the evidence for reoperation and pain as harms to be insufficient given the small number outcomes available for analysis.

Table B. Strength of the evidence for studies addressing surgical approaches for ankyloglossia

Outcome Number of Studies and Quality (Total Participants)	Study Limitations	Consistency	Directness	Precision	Reporting Bias	Finding/Strength of the Evidence
Breastfeeding Outcomes						
Nipple pain RCT: 3 good, [10, 11, 13] 1 poor[14] (251) Retrospective cohort: 1 poor[15] (367)	Low	Inconsistent	Direct	Imprecise	Undetected	Low SOE for an immediate reduction in nipple pain post-procedure due to inconsistent results across small studies.
Breastfeeding effectiveness RCTs-LATCH: 2 good, [10, 11]1poor[14] (193) IBFAT: 1 good [13] (58) BSES: 1 fair[10] (107) Retrospective cohort: 1 poor[15] (367)	Low	Inconsistent	Direct	Imprecise	Undetected	Low SOE for improved breastfeeding. Mothers consistently reported improved breastfeeding effectiveness, but outcome measures were heterogeneous and very short term. Observer-rated measures did not show significant improvements. Future studies could provide additional data to confirm or change the measure of effectiveness.
Length of breastfeeding Retrospective cohort: 1 poor [15](367)	High	NA	Direct	Imprecise	Undetected	Insufficient SOE due to the high risk of bias of the one retrospective study
Other Feeding Outcomes						
Feeding outcomes RCT: 1 poor [12](57) Retrospective cohort: 1 poor[16] (104)	High	Consistent	Indirect	Imprecise	Undetected	Insufficient SOE for all feeding outcomes given small number of participants, lack of standard outcome measures, and poor quality of studies.

Table B. Strength of the evidence for studies addressing surgical approaches for ankyloglossia (continued)

Outcome Number of Studies and Quality (Total Participants)	Study Limitations	Consistency	Directness	Precision	Reporting Bias	Finding/Strength of the Evidence
Speech Outcomes						
Speech and articulation Retrospective cohort: 1 poor[16] (104) Prospective cohort: 1 poor [18] (23)	High	Inconsistent	Indirect	Imprecise	Undetected	Insufficient SOE based on 2 poor quality cohort studies
Oral motor skills Retrospective cohort: 1 poor[16] (104) Prospective cohort: 1 poor [18] (23)	High	Consistent	Indirect	Imprecise	Undetected	Insufficient SOE based on 2 poor quality cohort studies
Social Outcomes						
Social concerns Retrospective cohort: 1 poor [16](104)	High	NA	Indirect	Imprecise	Undetected	Insufficient SOE based on 1 poor quality cohort study
Tongue mobility RCT: 1 poor[19] (16) Retrospective cohort: 1 poor [18](15)	High	Consistent	Direct	Imprecise	Undetected	Insufficient SOE based on 2 small, poor quality studies

Table B. Strength of the evidence for studies addressing surgical approaches for ankyloglossia (continued)

Outcome Number of Studies and Quality (Total Participants)	Study Limitations	Consistency	Directness	Precision	Reporting Bias	Finding/Strength of the Evidence
Harms						
Bleeding RCT: 1 poor[11](60) Case series: 14 poor[17, 22, 25, 28-38], 2 good[27, 39] (963)	High	Consistent	Direct	Imprecise	Suspected	Moderate SOE for minimal and short-lived bleeding based on an extensive search for harms reports in addition to the comparative data. Studies consistently reported minimal to no bleeding..
Reoperation RCT: 1 poor [10](107) Retrospective cohort: 1 poor[15] (367) Case series:1 good, [39] 4 poor[23, 24, 40, 41] (4080)	High	Consistent	Direct	Imprecise	Suspected	Insufficient SOE due to very small numbers of the outcome
Pain Case series: 2 good[27, 42] (84)	High	Consistent	Indirect	Imprecise	Suspected	Insufficient SOE for minimal, short-lived pain in infants. No studies reported excessive crying or an inability to feed soon after the intervention, but pain is arguably difficult to assess in infants, so outcomes were indirect and from poor quality or noncomparative studies.

BSES-SF=Breastfeeding Self-Efficacy Scale-Short Form; IBFAT=Infant Breastfeeding Assessment Tool; LATCH=Latch, Audible swallowing, Type of nipple, Comfort, Hold; RCT=randomized controlled trial; SOE=strength of the evidence

Applicability

Newborns referred for treatment of ankyloglossia were born primarily at tertiary care centers and recognized as having difficulty with breastfeeding concomitant with ankyloglossia. Most infants are not born at tertiary care centers; thus extrapolation to other birthing sites may not be possible. Moreover, newborns of mothers not choosing to breastfeed may not be recognized as having and/or diagnosed with ankyloglossia as breastfeeding difficulties were used as an indicator to evaluate for ankyloglossia. At minimum, the studies in this report only apply to

infants with both ankyloglossia and feeding difficulties; data on ankyloglossia absent feeding difficulties were unavailable.

In these studies, various clinicians were involved in making the ankyloglossia diagnoses; however, assessment of breastfeeding difficulty and diagnostic criteria for ankyloglossia were not universally described. Lack of a consistent objective measure to define and classify this condition may limit the reproducibility of findings. Furthermore, patients in these studies were between a median 6 days of age[13] and up to a mean 33 days of age (range 6 to 115) in another study.[11] Applicability to findings in older infants cannot be gleaned from this data; nor can durability of results.

Frenotomy was the only intervention employed in the good quality RCTs.[10, 11, 13] However, the specifics of the procedure were variably reported. As such the degree of posterior extension of the frenulum incision was not clearly defined and appears to be at the discretion and clinical expertise of the clinician. Also, the severity of the ankyloglossia was inconsistently reported, making inter-study generalizations difficult and, more importantly, limiting the broader applicability of findings.

The comparators used were sham surgery[11, 13] and no intervention.[10] Both no intervention and sham surgery are perhaps misnomers, however, since these infant-mother dyads underwent usual care, which could include, but is not limited to, lactation consultation, supportive care, and bottle-feeding advice.

The population studied in the question of benefit of ankyloglossia repair for social concerns included children and adults with wide variation in ages.

Research Gaps

Breastfeeding Outcomes

A critical unknown at this point is a good description of the natural history of ankyloglossia by severity, including long term risk of feeding, social and speech impediment. Future studies should consider direct comparisons of alternative treatments as currently available literature only addressed the comparison of frenotomy to sham. In order to conduct these studies, it would be helpful if the field could agree upon a standardized approach to identifying and classifying ankyloglossia; this would also improve our ability to synthesize the data across studies.

Given variation in outcomes that may be associated with earlier versus later frenotomy, future studies should assess timing of frenotomy to determine whether more significant reduction in maternal pain is achievable by earlier treatment and whether mothers are more apt to breastfeed longer if done earlier.

A significant gap in research is in understanding the durability of outcomes. Good quality comparative studies evaluated breastfeeding effectiveness immediately[11, 13] or within 5 days of frenotomy.[10] However, none adequately assessed whether effectiveness and other outcomes (e.g., changes in maternal nipple pain) were maintained months or, if appropriate, years later. Longer term follow up of both treated infants and controls is needed. Because there is so little available data on other feeding outcomes, this entire research question represents a gap and a potential area for future research.

Similarly, substantially more research is needed to consider whether treatment of ankyloglossia in infancy prevents future speech impediment as well as whether treatment later in life with frenotomy leads to improvement when speech problems arise. To conduct this research effectively, methods for evaluating risk and presence of speech impediment will need to be

standardized, and outcomes agreed upon. Understanding of the natural history of speech concerns in children with ankyloglossia is lacking as are comparative studies that utilize standardized measurement tools for speech outcomes.

No standard definitions of tongue mobility or established norms for mobility exist, and further research is needed to determine such parameters. Social concerns are difficult to measure objectively, so there will likely always be a subjective component to social outcomes. Larger studies that assess both treated and untreated individuals could provide useful data to minimize the potential bias found in the existing literature. Similarly, future research in objective measurement tools, or validated self-report tools, is needed.

Conclusions

A small body of evidence suggests that frenotomy may be associated with improvements in maternally reported breastfeeding effectiveness and nipple pain among infants with ankyloglossia and feeding difficulties. However, the available studies are small, data are inconsistently reported, and strength of the evidence is low to insufficient. Harms are typically minor, with the most common being self-limited bleeding. Research is lacking on nonsurgical interventions as well as on outcomes other than breastfeeding.

References

1. Lalakea ML, Messner AH. Ankyloglossia: does it matter? Pediatr Clin North Am. 2003 Apr;50(2):381-97. PMID: 12809329.
2. Suter VG, Bornstein MM. Ankyloglossia: facts and myths in diagnosis and treatment. J Periodontol. 2009 Aug;80(8):1204-19. PMID: 19656020.
3. Messner AH, Lalakea ML. Ankyloglossia: controversies in management. Int J Pediatr Otorhinolaryngol. 2000 Aug 31;54(2-3):123-31. PMID: 10967382.
4. Webb AN, Hao W, Hong P. The effect of tongue-tie division on breastfeeding and speech articulation: a systematic review. Int J Pediatr Otorhinolaryngol. 2013 May;77(5):635-46. PMID: 23537928.
5. Eunice Kennedy Shriver National Institute of Child Health and Human Development, National Institutes of Health (NIH), Department of Health & Human Services (DHHS). Preterm Labor and Birth: Condition Information [Internet]. Bethesda, MD: National Institute of Child Health and Human Development, National Institutes of Health, 2014. Available from: http://www.nichd.nih.gov/health/topics/preterm/conditioninfo/Pages/default.aspx. Accessed May 8, 2014
6. Higgins JPT, Green S. Cochrane Handbook for Systematic Reviews of Interventions The Cochrane Collaboration, 2011. Available from: http://www.cochrane-handbook.org. Accessed May 8, 2014
7. Viswanathan M, Berkman ND, Dryden DM. Assessing Risk of Bias and Confounding in Observational Studies of Interventions or Exposures: Further Development of the RTI Item Bank [Internet]. Rockville, MD: Agency for Healthcare Research and Quality, 2013. Available from: http://www.ncbi.nlm.nih.gov/books/NBK154461/.Accessed May 8, 2014
8. Santaguida P, Raina P. McMaster Quality Assessment Scale of Harms (McHarm) for primary studies: Manual for use of the McHarm. [Hamilton, ON: McMaster University, n.d.]
9. Methods Guide for Effectiveness and Comparative Effectiveness Reviews. Rockville, MD: Agency for Healthcare Research and Quality; January 2014. Available from: www.effectivehealthcare.ahrq.gov/ehc/products/60/318/CER-Methods-guide-140109.pdf. Accessed May 8, 2014
10. Emond A, Ingram J, Johnson D, et al. Randomised controlled trial of early frenotomy in breastfed infants with mild-moderate tongue-tie. Arch Dis Child Fetal Neonatal Ed. 2013 Nov 18;99(3):F189-95. PMID: 24249695.
11. Berry J, Griffiths M, Westcott C. A double-blind, randomized, controlled trial of tongue-tie division and its immediate effect on breastfeeding. Breastfeed Med. 2012 Jun;7(3):189-93. PMID: 21999476.
12. Hogan M, Westcott C, Griffiths M. Randomized, controlled trial of division of tongue-tie in infants with feeding problems. J Paediatr Child Health. 2005 May-Jun;41(5-6):246-50. PMID: 15953322.

13. Buryk M, Bloom D, Shope T. Efficacy of neonatal release of ankyloglossia: a randomized trial. Pediatrics. 2011 Aug;128(2):280-8. PMID: 21768318.

14. Dollberg S, Botzer E, Grunis E, et al. Immediate nipple pain relief after frenotomy in breast-fed infants with ankyloglossia: a randomized, prospective study. J Pediatr Surg. 2006 Sep;41(9):1598-600. PMID: 16952598.

15. Steehler MW, Steehler MK, Harley EH. A retrospective review of frenotomy in neonates and infants with feeding difficulties. Int J Pediatr Otorhinolaryngol. 2012 Sep;76(9):1236-40. PMID: 22704670.

16. Walls A, Pierce M, Wang H, et al. Parental perception of speech and tongue mobility in three-year olds after neonatal frenotomy. Int J Pediatr Otorhinolaryngol. 2014 Jan;78(1):128-31. PMID: 24315215.

17. Miranda BH, Milroy CJ. A quick snip - A study of the impact of outpatient tongue tie release on neonatal growth and breastfeeding. J Plast Reconstr Aesthet Surg. 2010 Sep;63(9):e683-5. PMID: 20493791.

18. Dollberg S, Manor Y, Makai E, et al. Evaluation of speech intelligibility in children with tongue-tie. Acta Paediatr. 2011 Sep;100(9):e125-7. PMID: 21401716.

19. Heller J, Gabbay J, O'Hara C, et al. Improved ankyloglossia correction with four-flap Z-frenuloplasty. Ann Plast Surg. 2005 Jun;54(6):623-8. PMID: 15900148.

20. Marchesan IQ, Martinelli RL, Gusmao RJ. Lingual frenulum: changes after frenectomy. J Soc Bras Fonoaudiol. 2012;24(4):409-12. PMID: 23306695.

21. Glynn RW, Colreavy M, Rowley H, et al. Division of tongue tie: review of practice through a tertiary paediatric otorhinolaryngology service. Int J Pediatr Otorhinolaryngol. 2012 Oct;76(10):1434-6. PMID: 22810118.

22. Choi YS, Lim JS, Han KT, et al. Ankyloglossia correction: Z-plasty combined with genioglossus myotomy. J Craniofac Surg. 2011 Nov;22(6):2238-40. PMID: 22134257.

23. Klockars T, Pitkaranta A. Pediatric tongue-tie division: indications, techniques and patient satisfaction. Int J Pediatr Otorhinolaryngol. 2009 Oct;73(10):1399-401. PMID: 19660817.

24. Yeh ML. Outpatient division of tongue-tie without anesthesia in infants and children. World J Pediatr. 2008 May;4(2):106-8. PMID: 18661764.

25. Lalakea ML, Messner AH. Ankyloglossia: the adolescent and adult perspective. Otolaryngol Head Neck Surg. 2003 May;128(5):746-52. PMID: 12748571.

26. Dave J, Sinha V, Barot D, et al. Speech disorders encountered in routine ENT practice and the role of speech therapy in its effective management. Indian Journal of Otology. 2013 October-December;19(4):169-72. PMID: 2014054877.

27. Puthussery FJ, Shekar K, Gulati A, et al. Use of carbon dioxide laser in lingual frenectomy. Br J Oral Maxillofac Surg. 2011 Oct;49(7):580-1. PMID: 20728254.

28. Messner AH, Lalakea ML. The effect of ankyloglossia on speech in children. Otolaryngol Head Neck Surg. 2002 Dec;127(6):539-45. PMID: 12501105.

29. Srinivasan A, Dobrich C, Mitnick H, et al. Ankyloglossia in breastfeeding infants: the effect of frenotomy on maternal nipple pain and latch. Breastfeed Med. 2006 Winter;1(4):216-24. PMID: 17661602.

30. Blenkinsop A. A measure of success: audit of frenulotomy for infant feeding: problems associated with tongue-tie. MIDIRS Midwifery Digest. 2003;13(3):389-92.

31. Ridgers I, McCombe K, McCombe A. A tongue-tie clinic and service. Br J Midwifery. 2009;17(4):230-3.

32. Sethi N, Smith D, Kortequee S, et al. Benefits of frenulotomy in infants with ankyloglossia. Int J Pediatr Otorhinolaryngol. 2013 May;77(5):762-5. PMID: 23453795.

33. Geddes DT, Langton DB, Gollow I, et al. Frenulotomy for breastfeeding infants with ankyloglossia: effect on milk removal and sucking mechanism as imaged by ultrasound. Pediatrics. 2008 Jul;122(1):e188-94. PMID: 18573859.

34. Wallace H, Clarke S. Tongue tie division in infants with breast feeding difficulties. Int J Pediatr Otorhinolaryngol. 2006 Jul;70(7):1257-61. PMID: 16527363.

35. Amir LH, James JP, Beatty J. Review of tongue-tie release at a tertiary maternity hospital. J Paediatr Child Health. 2005 May-Jun;41(5-6):243-5. PMID: 15953321.

36. Fiorotti RC, Bertolini MM, Nicola JH, et al. Early lingual frenectomy assisted by CO2 laser helps prevention and treatment of functional alterations caused by ankyloglossia. Int J Orofacial Myology. 2004 Nov;30:64-71. PMID: 15832863.

37. Ballard JL, Auer CE, Khoury JC. Ankyloglossia: assessment, incidence, and effect of frenuloplasty on the breastfeeding dyad. Pediatrics. 2002 Nov;110(5):e63. PMID: 12415069.

38. Masaitis NS, Kaempf JW. Developing a frenotomy policy at one medical center: a case study approach. J Hum Lact. 1996 Sep;12(3):229-32. PMID: 9025430.

39. Argiris K, Vasani S, Wong G, et al. Audit of tongue-tie division in neonates with breastfeeding difficulties: how we do it. Clin Otolaryngol. 2011 Jun;36(3):256-60. PMID: 21752209.

40. O'Callahan C, Macary S, Clemente S. The effects of office-based frenotomy for anterior and posterior ankyloglossia on breastfeeding. Int J Pediatr Otorhinolaryngol. 2013 May;77(5):827-32. PMID: 23523198.

41. Hong P, Lago D, Seargeant J, et al. Defining ankyloglossia: a case series of anterior and posterior tongue ties. Int J Pediatr Otorhinolaryngol. 2010 Sep;74(9):1003-6. PMID: 20557951.

42. Mettias B, O'Brien R, Abo Khatwa MM, et al. Division of tongue tie as an outpatient procedure. Technique, efficacy and safety. Int J Pediatr Otorhinolaryngol. 2013 Apr;77(4):550-2. PMID: 23411135.

Introduction

Background

Ankyloglossia

Ankyloglossia is a congenital condition in which a neonate is born with an abnormally short, thickened, or tight lingual frenulum that restricts mobility of the tongue. While it can be associated with other craniofacial abnormalities, it is most often an isolated anomaly.[1] It variably causes reduced tongue mobility and has been associated with functional limitations in breastfeeding, swallowing, articulation, orthodontic problems including malocclusion, open bite, and separation of lower incisors, mechanical problems related to oral clearance, and psychological stress. Reported rates range from 2.1 to 10.7 percent,[2] but definitive incidence and prevalence statistics are difficult to obtain because there criterion standard or clinically practical diagnostic criteria.

Anterior ankyloglossia is defined as tongue-tie with a prominent lingual frenulum and/or restricted tongue protrusion with tongue tip tethering. The diagnosis of posterior ankyloglossia is considered when the lingual frenulum is not very prominent on inspection but is thought to be tight on manual palpation or is found to be abnormally prominent, short, thick, or fibrous cord-like with the use of the grooved director. Although treatment is similar in anterior and posterior cases, posterior ankyloglossia is more subtle in presentation. Usually, clinicians recognize the anterior frenulum as the cause of ankyloglossia; however, an infant can have ankyloglossia even without obvious abnormalities of the anterior frenulum. Anterior ankyloglossia has been found more commonly in males and posterior ankyloglossia in females.[3] Posterior ankyloglossia is more likely to require revision surgery due to the relative difficulty of accurate diagnosis and treatment.

Estimates in the literature of the number of infants with ankyloglossia who have feeding difficulties are based on small case series without control groups. Mechanistically, infants with restrictive ankyloglossia cannot extend their tongues over the lower gum line to form a proper seal and therefore use their jaws to keep the breast in the mouth for breastfeeding. Adequate tongue mobility is required, and infants with ankyloglossia often cannot overcome their deficiency with conservative measures such as positioning and latching techniques.[2] Ineffective latch associated with ankyloglossia is hypothesized to underlie breastfeeding problems in these infants including failure to thrive, maternal nipple damage, maternal breast pain, poor milk supply, maternal breast engorgement, and refusing the breast.[2]

Nonetheless, consensus on ankyloglossia's role in breastfeeding difficulties is lacking. A minority of surveyed pediatricians (10%) and otolaryngologists (30%) believe it commonly affects feeding, while 69 percent of lactation consultants feel that it frequently causes breastfeeding problems.[4] Therefore, depending on the audience, enthusiasm for its treatment varies. Currently, the National Health Service (NHS) and the Canadian Paediatric Society (CPS) recommend treatment only if it interferes with breastfeeding.[5] Unfortunately, a standard definition of "interference" with breastfeeding is not provided, leaving room for interpretation and variation in treatment thresholds. The absence of data on the natural history of untreated ankyloglossia creates even more uncertainty. Some propose that a short frenulum elongates spontaneously due to progressive stretching and thinning of the frenulum with age and use.[1] However, there are no prospective longitudinal data on the fate of the congenitally short lingual

frenulum. Without this information it is difficult to inform parents fully about the long-term implications of ankyloglossia, which complicates the decision making process.

Although most ankyloglossia research is focused on the infant and breastfeeding issues, concerns beyond infancy include speech-related issues, such as difficulty with articulation, and social concerns related to limited tongue mobility. Individuals with untreated ankyloglossia may experience difficulty with licking foods such as ice cream, kissing, drooling, playing wind instruments, and licking the lips. Self- esteem or psychological issues may also be a concern for affected older patients.

Treatment Strategies

Surgical Approaches

Surgical modalities include frenotomy, frenulectomy, and tongue tie release surgery. These interventions are often not clearly differentiated in the literature but involve clipping or cutting of the lingual frenulum using the proceduralist's fingers, a grooved tongue director, or other instrument to lift the tongue, which puts the tension on the frenulum and using straight scissors to divide the frenulum, generally without sedation. Laser frenotomy or frenulotomy has also been described,[6] and proponents argue that its use is more exact and provides better hemostasis than standard frenotomy or frenulotomy.

Frenuloplasty is more technically involved than frenotomy or frenulotomy. It generally refers to rearranging tissue or adding grafts after making incisions and closing the resultant wound in a specific pattern to lengthen the anterior tongue. Specific types of frenuloplasty include Z-frenuloplasty, which involves making a longitudinal incision along the length of the lingual frenulum combined with perpendicular incisions at tongue tip and floor of the mouth. These cuts create a Z-type incision. Submucosal flaps are then elevated, and transposed flaps are sutured closed, resulting in increased tongue length and mobility. A second type of frenuloplasty involves a horizontal division at the base of the frenulum where a harvested buccal mucosal graft is inserted and affixed to fill the defect created by the incision. Horizontal-to-vertical frenuloplasty is a third type in which a horizontal incision is created at mid-frenulum to release the tethering fibrotic band. The incision is then converted to a vertical orientation and closed with sutures to effectively elongate the anterior tongue. Frenuloplasty is most commonly performed under a general anesthetic and used in older infants and children or in more complex frenulum repairs.

Nonsurgical Approaches

Nonsurgical approaches include speech therapy and lactation interventions and observation to determine if intervention is warranted (Table 1).

Table 1. Nonsurgical treatment approaches

Intervention	Description
Complementary and alternative procedures	Diverse group of therapies not conventionally practiced by physicians or allied health professionals (e.g., craniosacral therapy).
Lactation intervention	Counseling and recommendations from a lactation consultant for better, easier or more efficient breast-feeding. Focus on latching technique and infant and maternal positioning on breast.
Physical therapy/occupational therapy	Approaches to reduce tension in and stretch neck, back, and strap muscles to improve range of motion. This includes myofascial release and other manual techniques.
Speech therapy/oromotor therapy	Exercises and techniques intended to develop awareness, strength, coordination and mobility of the oral muscles including the tongue, lip, and palate. Evaluation and treatment of swallowing and speech disorders using specific exercises and procedures.
Observation	Supportive therapy for mother without any treatment approach and observation for improvement through natural history of the condition process.

Several measures have been developed to assess the severity of ankyloglossia. Structured assessments can also be used to assess the effectiveness of breastfeeding. Table 2 outlines measures used in the studies reported in this review.

Table 2. Structured assessments used in ankyloglossia literature

Measure	Description
Degree of Ankyloglossia	
Coryllos criteria	Scale for categorizing ankyloglossia based on proximity of frenulum attachment to tongue tip: Type 1=frenulum attached to tip of tongue. Type 2=frenulum attached 2-4 millimeters behind tongue tip on or behind alveolar ridge. Type 3=mid-tongue attachment. Type 4=attachment at base of tongue. Type 4 is associated with more difficulty with bolus swallowing and more significant symptoms.
Hazelbaker Assessment Tool for Lingual Frenulum Function (HATLFF)	Measure of ankyloglossia extent and severity that include items to assess the appearance and function of the tongue and frenulum. Lower scores indicate more severe ankyloglossia. HATLFF is scored: 0-14 with14=perfect; 11=acceptable if appearance item score is 10; <11=impaired function (frenotomy should be considered if management fails; frenotomy is necessary if appearance item score is <8). HATLFF score of 6-12=mild to moderate tongue-tie; <6=severe tongue-tie.[7, 8]
Breastfeeding Effectiveness	
Breastfeeding Self-Efficacy Scale (BSES)	Measure of maternal breastfeeding confidence that uses a 5-point (1=not at all confident to 5=always confident) Likert scale to assess agreement with statements such as “I can always position my baby correctly at my breast.” BSES scores range from 33-165 on the 33-item instrument [9] and 14-70 on the 14-item BSES-Short Form.[10] Higher overall scores indicate higher levels of breastfeeding self-efficacy.
Infant Breastfeeding Assessment Tool (IBFAT)	Measure of clinician or maternally rated perception of 4 items related to effectiveness of and satisfaction with a feeding (readiness to feed, rooting, latching on, sucking) rated on a 3-point scale (e.g., 3=rooted effectively at once, 0=did not root). Higher scores indicate greater perceived effectiveness. IBFAT scores range from 0-12; 12=vigorous and effective feeding.[11]

Table 2. Structured assessments used in ankyloglossia literature (continued)

Measure	Description
Latch, Audible swallowing, Type of nipple, Comfort, Hold (LATCH)	Measure of effectiveness of latch to the breast, feeding, comfort for mother, and maternal positioning rated on 3 levels with higher scores indicating greater effectiveness. LATCH score ≤8=breastfeeding difficulties.[12]

Scope and Key Questions

Scope of Review

This systematic review provides a comprehensive review of potential benefits of treatments (surgical and nonsurgical) as well as harms associated with those therapies in individuals with ankyloglossia and tight labial frenulum (lip-tie) concomitant with ankyloglossia. We assess outcomes related to breast and bottle-feeding and related to tongue tie in later life (e.g., orthodontic and dental issues, speech, self-esteem).

Key Questions

We have synthesized evidence in the published literature to address the following Key Questions (KQs):

KQ1. What are the benefits of various treatments in breastfeeding newborns and infants with ankyloglossia intended to improve breastfeeding outcomes? Surgical treatments include frenotomy (anterior and/or posterior), frenuloplasty (transverse to vertical frenuloplasty), laser frenulectomy/frenulotomy, and Z-plasty repair. Nonsurgical treatments include complementary and alternative medicine (CAM) therapies (e.g. craniosacral therapy), lactation intervention, physical/occupational therapy, oral motor therapy, and stretching exercises/therapy.

KQ2a. What are the benefits of various treatments in newborns, infants, and children with ankyloglossia intended to prevent, mitigate, or remedy attributable medium and long-term *feeding* sequelae including trouble bottle feeding, spilling and dribbling, difficulty moving food boluses in the mouth and deglutition?

KQ2b. What are the benefits of various treatments in infants and children with ankyloglossia intended to prevent, mitigate, or remedy attributable medium and long term *other* sequelae including articulation disorders, poor oral hygiene, oral and oropharyngeal dysphagia, sleep disordered breathing, orthodontic issues including malocclusion, open bite due to reverse swallowing, lingual tipping of the lower central incisors, separation of upper central incisors, crowding, narrow palatal arch, and dental caries?

KQ3. What are the benefits of various treatments for ankyloglossia in children up to 18 years of age intended to prevent or address social concerns related to tongue mobility (i.e., speech, oral hygiene, excessive salivation, kissing, spitting while talking, and self-esteem)?

KQ4. What are the benefits of simultaneously treating ankyloglossia and concomitant tight labial frenulum (lip-tie) in infants and children up to age 18 intended to improve or remedy

breastfeeding, articulation, orthodontic and dental, and other feeding outcomes? What are the relative benefits of treating only ankyloglossia when tight labial frenulum (lip-tie) is also diagnosed?

KQ5. What are the harms of treatments for ankyloglossia or ankyloglossia with concomitant lip-tie in neonates, infants, and children up to age 18?

Table 3 outlines the population, intervention, comparator, outcomes, timing, and setting characteristics for each KQ.

Table 3. PICOTS

PICOTS	Criteria
Population	• KQ1: Breastfeeding newborns with ankyloglossia • KQ2 and KQ3: Infants and children with ankyloglossia • KQ4: Infants and children (newborns up to 18 years of age) with ankyloglossia and concomitant tight labial frenulum (lip-tie) KQ5: Children up to age 18 treated for ankyloglossia or ankyloglossia and concomitant lip-tie.
Intervention(s)	• Surgical interventions, including frenotomy (anterior or posterior), frenuloplasty, laser frenulectomy and Z-plasty repair • Nonsurgical treatments include complementary and alternative medicine (CAM) therapies (e.g. craniosacral therapy), lactation intervention, and speech therapy (for children ages 2 to 18 years), physical/occupational therapy, oral motor therapy, and stretching exercises/therapy
Comparator	• Other surgical approach • Non-surgical interventions including lactation intervention, speech therapy, physical/occupational therapy oral motor therapy, and stretching exercises/therapy • Observation • Complementary and alternative medicine (CAM) therapies (e.g. craniosacral therapy) • Placebo (sham therapy)
Outcomes	• Breastfeeding, including latch, nipple pain, nipple excoriations, nipple infections (mastitis), weight gain, aerophagia, swallowing function, failure to thrive, milk transfer, low milk supply, breastfeeding cessation • Other feeding issues, including difficulty bottle feeding, moving food boluses in the mouth, deglutition, spilling and dribbling, reflux • Articulation • Speech (e.g., speech fluency, effort with speech, speech intelligibility) • Sleep disordered breathing (sleep apnea) • Oral hygiene • Excessive salivation • Orthodontic problems, including malocclusion, open bite due to reverse swallowing, lingual tipping of lower central incisors, separation of upper central incisors, crowding, and narrow palatal arch, dental caries • Psychological (e.g., self-esteem) • Harms, including excessive bleeding, airway obstruction, pain, transient poor feeding secondary to discomfort, dysphagia, complications related to dysphagia such as aspiration pneumonia, surgical site infection, nerve damage, salivary gland damage, ranulae, scarring, soft tissue damage, oral aversion, readherence, and need for further surgery/revision
Timing	• Short-term (breastfeeding) • Long-term (feeding) speech, psychological, oral hygiene
Setting	• Inpatient or outpatient pediatric care, operating room, newborn nursery or NICU, ENT clinic, primary care outpatient, dental office, breastfeeding medicine clinic

CAM=Complementary and alternative medicine; ENT=ear, nose and throat; KQ=Key Question; NICU= Neonatal intensive care unit; PICOTS=Population, Intervention, Comparator, Outcomes, Timing, Setting

Analytic Framework

Figure 1 depicts Key Questions 1, 4, and 5 within the context of the PICOTS described in the document. The figure examines surgical and nonsurgical treatments in newborns and infants to improve breastfeeding outcomes. Intermediate outcomes include maternal nipple pain, ability to latch and maintain latch, tongue mobility, and aerophagia. Final outcomes include duration of breastfeeding, failure to thrive, infant weight gain and oral and oropharyngeal dysphagia. Harms (KQ5) may occur at any point after the intervention is received.

Figure 1. Analytic framework for ankyloglossia in neonates and infants

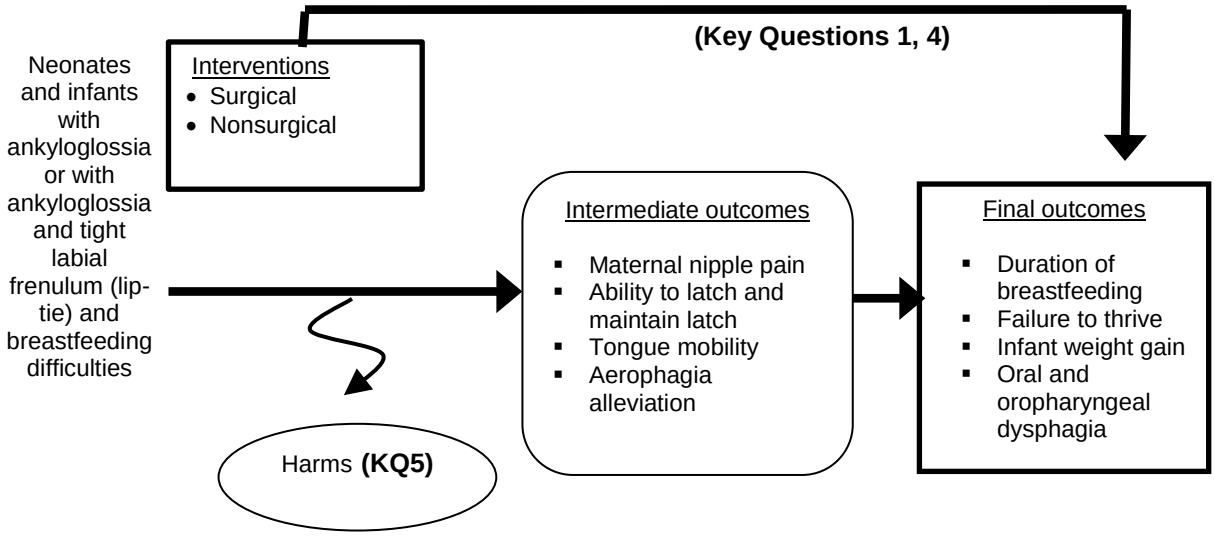
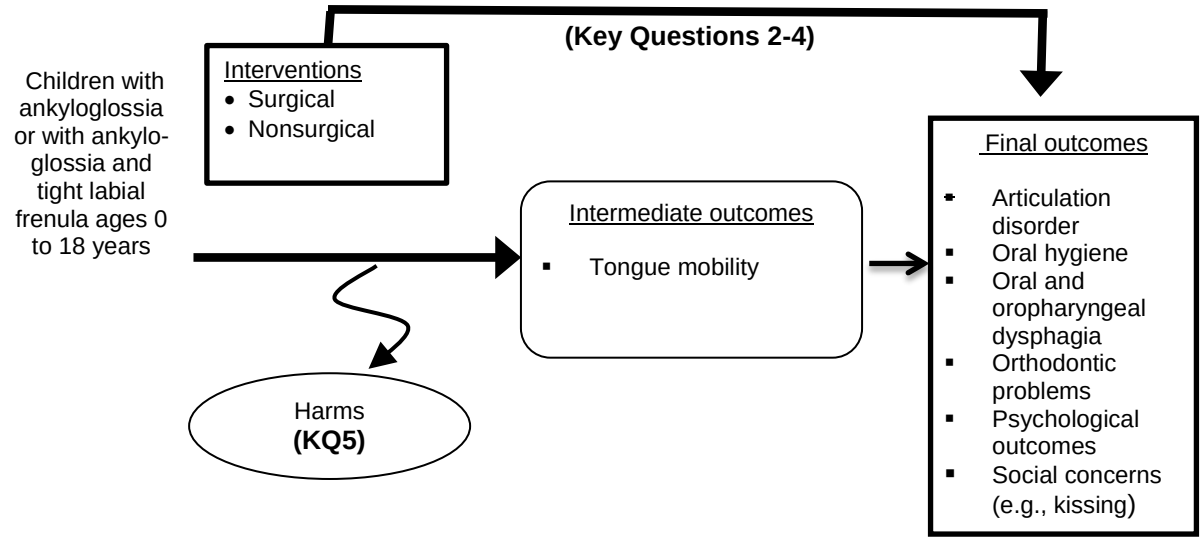


Figure 2 depicts Key Questions 2, 3, 4, and 5 within the context of the PICOTS described in the document. The figure examines surgical and nonsurgical treatments in infants and children with ankyloglossia (KQ2, KQ3) or ankyloglossia with concomitant tight labial frenulum (lip-tie) (KQ4). The intermediate outcome is tongue mobility and final health outcomes include articulation disorder, oral hygiene, oral and oropharyngeal dysphagia, orthodontic problems, psychological outcomes and social concerns including kissing. Harms (KQ5) may occur at any point after the intervention is received.

Figure 2. Analytic framework for ankyloglossia in infants and children up to 18 years of age



Organization of This Report

The Methods section describes our processes including our search strategy, inclusion and exclusion criteria, approach to review of abstracts and full publications, and methods for extraction of data into evidence tables, and compiling evidence. We also describe our approach to grading the quality of the literature and to describing the strength of the body of evidence.

The Results section presents the findings of the literature search and the review of the evidence by key question, synthesizing the findings across strategies.

The Discussion section of the report discusses the results and expands on the methodologic considerations relevant to each key question. We also outline the current state of the literature and challenges for future research in the field.

The report includes a number of appendices to provide further detail on our methods and the studies assessed. The appendices are as follows:

- Appendix A: Search Strategies
- Appendix B: Sample Abstract and Full Text Review Forms
- Appendix C: List of Excluded Studies
- Appendix D: Evidence Tables
- Appendix E: Quality Screening Tools
- Appendix F: Quality Scoring Results
- Appendix G: Case Reports of Harms
- Appendix H: Conference Abstract Results
- Appendix I: Applicability

We also include a list of abbreviations and acronyms at the end of the report.

Uses of This Evidence Report

We anticipate this report will be of primary value to organizations that develop guidelines for clinical practitioners and to health care providers who take care of infants and children up to 18 years of age with ankyloglossia. Interested organizations would include the American Academy of Pediatrics, the Pediatric Academic Societies (PAS), the Academy of Breastfeeding Medicine

(ABM), the American Academy of Pediatric Dentistry (AAPD), the American Academy of Otolaryngology—Head and Neck Surgery (AAO-HNS), the American Speech-Language-Hearing Association (ASHA), the International Lactation Consultant Association (ILCA), Lactation Consultants of Australia and New Zealand (LCANZ), the College of Lactation Consultants of Western Australia (CLCWA), the American Orthodontic Society (AOS) and the American Association of Orthodontists (AAO), the National Health Service (NHS) and other organizations and societies for pediatric care. Ankyloglossia is diagnosed and treated by an array of physicians and allied health professionals, but this most commonly includes pediatricians, otolaryngologists, dentists, and lactation consultants. This report supplies practitioners and researchers up-to-date information about the current state of evidence, and assesses the quality of studies that aim to determine the outcomes of treatments for ankyloglossia. It will be of interest to parents concerned about the health of their infants and facing treatment choices around care for their children with ankyloglossia.

Researchers can obtain a concise analysis of the current state of knowledge in this field. They will be poised to pursue further investigations that are needed to advance research methods, develop new treatment strategies, and optimize the effectiveness and safety of clinical care infants and children up to 18 years of age with ankyloglossia.

Methods

In this chapter, we document the procedures that the Vanderbilt Evidence-based Practice Center (EPC) used to produce a comparative effectiveness review (CER) on the approaches to treatment for ankyloglossia. These procedures follow the methods suggested in the Agency for Healthcare Research and Quality (AHRQ) Effective Health Care Program *Methods Guide for Effectiveness and Comparative Effectiveness Reviews*.[13]

Topic Refinement and Review Protocol

The topic for this report was nominated by the American Academy of Pediatrics in a public process using the Effective Health Care Web site. Working from the nomination, we drafted the initial key questions (KQs) and analytic framework and refined them with input from key informants representing the fields of pediatric care, pediatric otolaryngology, breastfeeding and lactation, dentistry, occupational therapy, and speech therapy. All members of the research team were required to submit information about potential conflicts of interest before initiation of the work. No members of the review team had any conflicts.

After review from AHRQ, the questions and framework were posted online for public comment. No changes to the questions or framework were recommended. We also developed population, interventions, outcomes, timing, and settings (PICOTS) criteria for intervention KQs.

We identified technical experts on the topic to provide assistance during the project. The Technical Expert Panel (TEP), representing the fields of pediatric care, pediatric otolaryngology, breastfeeding and lactation, dentistry, and speech-language pathology, contributed to the AHRQ's broader goals of (1) creating and maintaining science partnerships as well as public-private partnerships and (2) meeting the needs of an array of potential customers and users of its products. Thus, the TEP was both an additional resource and a sounding board during the project. The TEP included nine members serving as technical or clinical experts. To ensure robust, scientifically relevant work, we called on the TEP to review and provide comments as our work progressed. TEP members participated in conference calls and discussions through e-mail to:

- Help to refine the analytic framework and KQs at the beginning of the project;
- Discuss the preliminary assessment of the literature, including inclusion/exclusion criteria; and
- Provide input on the information and domains included in evidence tables.

The final protocol was posted to the AHRQ Effective Health Care Web site.[14]

Literature Search Strategy

Search Strategy

To ensure comprehensive retrieval of relevant studies of therapies for children with ankyloglossia or ankyloglossia with concomitant tight labial frenulum (lip-tie), we used four key databases: the MEDLINE® medical literature database via the PubMed® interface, the PsycINFO® psychology and psychiatry database, the Cumulative Index of Nursing and Allied Health Literature (CINAHL®) and EMBASE (Excerpta Medica Database), an international biomedical and pharmacological literature database via the Ovid® interface. Search strategies applied a combination of controlled vocabulary (Medical Subject Headings (MeSH), PsycINFO headings, CINAHL medical headings, and Emtree headings, respectively) to focus specifically

on concepts related to ankyloglossia and its treatment as well as treatment harms. Literature searches were not restricted to a year range (i.e., searches were from inception of the database to the present) given the need to capture variations in practice patterns and trends in breastfeeding over time.

We included studies published in English only as a review of non-English citations retrieved by our MEDLINE search identified few studies of relevance. Appendix A lists our search terms and strategies and the yield from each database. Searches were executed between September 2013 and May 2014**.**

We carried out hand searches of the reference lists of recent systematic reviews or meta-analyses of therapies for ankyloglossia; the investigative team scanned the reference lists of articles included after the full-text review phase for studies that potentially could meet our inclusion criteria.

As we did not review medications or devices, we did not request Scientific Information Packets or regulatory information. We reviewed abstracts presented at annual meetings of key scientific societies including the American Association of Pediatrics (AAP), the Pediatric Academic Societies (PAS), the Academy of Breastfeeding Medicine (ABM), the American Academy of Pediatric Dentistry (AAPD), the American Academy of Otolaryngology—Head and Neck Surgery (AAO-HNS), the American Speech-Language-Hearing Association (ASHA), the International Lactation Consultant Association (ILCA), Lactation Consultants of Australia and New Zealand (LCANZ), the College of Lactation Consultants of Western Australia (CLCWA), the American Orthodontic Society (AOS) and the American Association of Orthodontists (AAO). We identified relevant theses and dissertations through ProQuest Dissertations and Theses (PQDT).

Inclusion and Exclusion Criteria

Table 4 lists the inclusion/exclusion criteria we used based on our understanding of the literature, key informant and public comment during the topic-refinement phase, input from the TEP, and established principles of systematic review methods.

Table 4. Inclusion and exclusion criteria

Category	Criteria
Study population	Inclusion: Children ages 0-18 with ankyloglossia or ankyloglossia with concomitant tight labial frenulum (lip-tie); Exclusion: Studies with participants with Van der Woude syndrome, Pierre Robin syndrome, Down syndrome, or craniofacial abnormalities were excluded as were studies of premature babies (<37 weeks of gestation[15])
Publication languages	Inclusion: English Exclusion: Non-English
Admissible evidence (study design and other criteria)	Included study designs RCTs, prospective and retrospective cohort studies, nonrandomized controlled trials, prospective and retrospective case series, and cross over studies Case reports to assess harms Other criteria Original research studies providing sufficient detail regarding methods and results to enable use and aggregation of the data and results Studies must address one or more of the following: • Surgical interventions (simple anterior frenectomy, laser frenulectomy, posterior frenulectomy, Z-plasty repair) • Nonsurgical treatments include complementary and alternative medicine (CAM) therapies (e.g. craniosacral therapy, myofascial release, and other chiropractic therapies), lactation intervention , speech therapy, physical therapy, oral motor therapy and stretching exercises/therapy • Baseline and outcome data (including harms) related to interventions for ankyloglossia Relevant outcomes must be able to be extracted from data in the papers Data must be presented in the aggregate (vs. individual participant data)

CAM=complementary and alternative medicine; RCT=randomized controlled trial

Study Selection

Once we identified articles through the electronic database searches and hand-searching, we examined abstracts of articles to determine whether studies met our criteria. Two reviewers separately evaluated the abstracts for inclusion or exclusion, using an Abstract Review Form (Appendix B). If one reviewer concluded that the article could be eligible for the review based on the abstract, we retained it. Following abstract review, two reviewers independently assessed the full text of each included study using a standardized form (Appendix B) that included questions stemming from our inclusion/exclusion criteria. Disagreements between reviewers were resolved by a senior reviewer. All abstract and full text reviews were conducted using the DistillerSR online screening application (Evidence Partners Incorporated, Ottawa, Ontario). Excluded studies, and the reasons for exclusion, are presented in Appendix C.

Data Extraction

The staff members and clinical experts who conducted this review jointly developed the evidence tables. We designed the tables to provide sufficient information to enable readers to understand the studies and to determine their quality; we gave particular emphasis to essential information related to our key questions. Two evidence table templates were employed to facilitate the extraction of data based on study type; one form was designed for case series and

one to accommodate all types of comparative studies. We based the format of our evidence tables on successful designs used for prior systematic reviews.

The team was trained to extract data by extracting several articles into evidence tables and then reconvening as a group to discuss the utility of the table design. We repeated this process through several iterations until we decided that the tables included the appropriate categories for gathering the information contained in the articles. All team members shared the task of initially entering information into the evidence tables. A second team member also reviewed the articles and edited all initial table entries for accuracy, completeness, and consistency. The two data extractors reconciled disagreements concerning the information reported in the evidence tables. The full research team met regularly during the article extraction period and discussed global issues related to the data extraction process. In addition to outcomes related to intervention effectiveness, we extracted all data available on harms. Harms encompass the full range of specific negative effects, including the narrower definition of adverse events.

The final evidence tables are presented in their entirety in Appendix D. Studies are presented in the evidence tables alphabetically by the last name of the first author. A list of abbreviations and acronyms used in the tables appears at the beginning of that appendix.

Data Synthesis

We considered the possibility of conducting a meta-analysis, but the small number of the studies, the study designs and the heterogeneity of interventions and outcomes made a meta-analysis inappropriate. We completed evidence tables for all included studies, and data are presented in summary tables and analyzed qualitatively in the text.

Quality (Risk of Bias) Assessment of Individual Studies

We used four tools to assess quality of individual studies: the Cochrane Risk of Bias Tool for Randomized Controlled Trials,[16] a cohort study assessment instrument and a tool for case series, both adapted from RTI Item Bank questions,[17] and a four-item harms assessment instrument for cohort studies derived from the McMaster Quality Assessment Scale of Harms (McHarm) for Harms Outcomes[18] and the RTI Item Bank.[17]

The Cochrane Risk of Bias tool is designed for the assessment of studies with experimental designs and randomized participants. Fundamental domains include sequence generation, allocation concealment, blinding, completeness of outcome data, and selective reporting bias. The RTI Item Bank-based cohort instrument was used to assess the quality of nonrandomized studies (e.g., cohort and case-control studies). Questions assess selection and follow up of study groups, the comparability of study groups, and the ascertainment of outcomes of interest for cohort studies. The case series tool assesses attrition, blinding, appropriateness of outcome measures, and reporting bias. The harms assessment tool documents whether harms were predefined and pre-specified and if standard scales were applied. We did not assess the quality of case reports, which we used solely for harms data. All four tools are presented in Appendix E.

Quality assessment of each study was conducted by two team members independently using the forms presented in Appendix E. Any discrepancies were adjudicated through discussion between the assessors to reach consensus or via a senior reviewer. Investigators did not rely on the study design as described by authors of individual papers; rather, the methods section of each paper was reviewed to determine which rating tool to employ. The results of these tools were then translated to the AHRQ standard of "good," "fair," and "poor" quality designations as described below.

Determining Quality Ratings

- We required that randomized controlled trials (RCTs) receive a positive score (i.e., low risk of bias for RCTs) on all questions used to assess quality to receive a rating of good (equivalent to low risk of bias). RCTs had to receive at least five positive scores to receive a rating of fair (moderate risk of bias), and studies with less than or equal to four positive ratings were considered poor quality (high risk of bias). We designated an "unclear" rating on an individual question as a positive rating as long as the consensus of the investigators assessing quality was that study outcomes were not likely to be biased by the factor.
- We required that cohort studies receive positive scores on all elements to receive a rating of good, less than or equal to two negative ratings for fair, and greater than two negative scores for a rating of poor quality.
- Case series, or pre-post studies, have inherently high risk of bias. Nonetheless, prospective case series that enroll participants consecutively and control for potentially confounding factors may provide more evidence to support comparative studies. We assessed case series using questions identified in the AHRQ Effective Health Care program's *Methods Guide for Effectiveness and Comparative Effectiveness Reviews*[13] but did not assign a quality level for these studies as it would be inappropriate to assess them on the same scale as prospective cohort and RCT designs. Rather, the elements on which they were scored and the results are presented in Appendix F.
- For harms assessment we required that studies receive a positive score (i.e., an affirmative response) on all four questions to receive a rating of good. Studies had to receive three positive scores to receive a rating of fair, and studies with less than three positive scores received a rating of poor.

Strength of the Body of Evidence

We applied explicit criteria for rating the overall strength of the evidence for each key intervention-outcome pair for which the overall risk of bias is not overwhelmingly high. We established concepts of the quantity of evidence (e.g., numbers of studies, aggregate ending-sample sizes), the quality of evidence (from the quality ratings on individual articles), and the coherence or consistency of findings across similar and dissimilar studies and in comparison to known or theoretically sound ideas of clinical or behavioral knowledge.

The strength of evidence evaluation is that stipulated in the Effective Health Care Program's *Methods Guide for Effectiveness and Comparative Effectiveness Reviews*[13] and in the updated strength of evidence guide[19] which emphasizes the following five major domains: study limitations (low, medium, high level of limitation), consistency (inconsistency not present, inconsistency present, unknown or not applicable), directness (direct, indirect), and precision (precise, imprecise), and reporting bias. Study limitations are derived from the quality assessment of the individual studies that addressed the KQ and specific outcome under consideration. Each key outcome for each comparison of interest is given an overall evidence grade based on the ratings for the individual domains.

The overall strength of evidence was graded as outlined in Table 5. Two senior staff independently graded the body of evidence; disagreements were resolved as needed through discussion or third-party adjudication. We recorded strength of evidence assessments in tables, summarizing results for each outcome.

Table 5. Strength of evidence grades and definitions*

Grade	Definition
High	**We are very confident that the estimate of effect lies close to the true effect for this outcome.** The body of evidence has few or no deficiencies. We believe that the findings are stable, i.e., another study would not change the conclusions.
Moderate	**We are moderately confident that the estimate of effect lies close to the true effect for this outcome.** The body of evidence has some deficiencies. We believe that the findings are likely to be stable, but some doubt remains.
Low	**We have limited confidence that the estimate of effect lies close to the true effect for this outcome.** The body of evidence has major or numerous deficiencies (or both). We believe that additional evidence is needed before concluding either that the findings are stable or that the estimate of effect is close to the true effect.
Insufficient	**We have no evidence, we are unable to estimate an effect, or we have no confidence in the estimate of effect for this outcome**. No evidence is available or the body of evidence has unacceptable deficiencies, precluding reaching a conclusion.

* Excerpted from Berkman et al. 2013[19]

Applicability

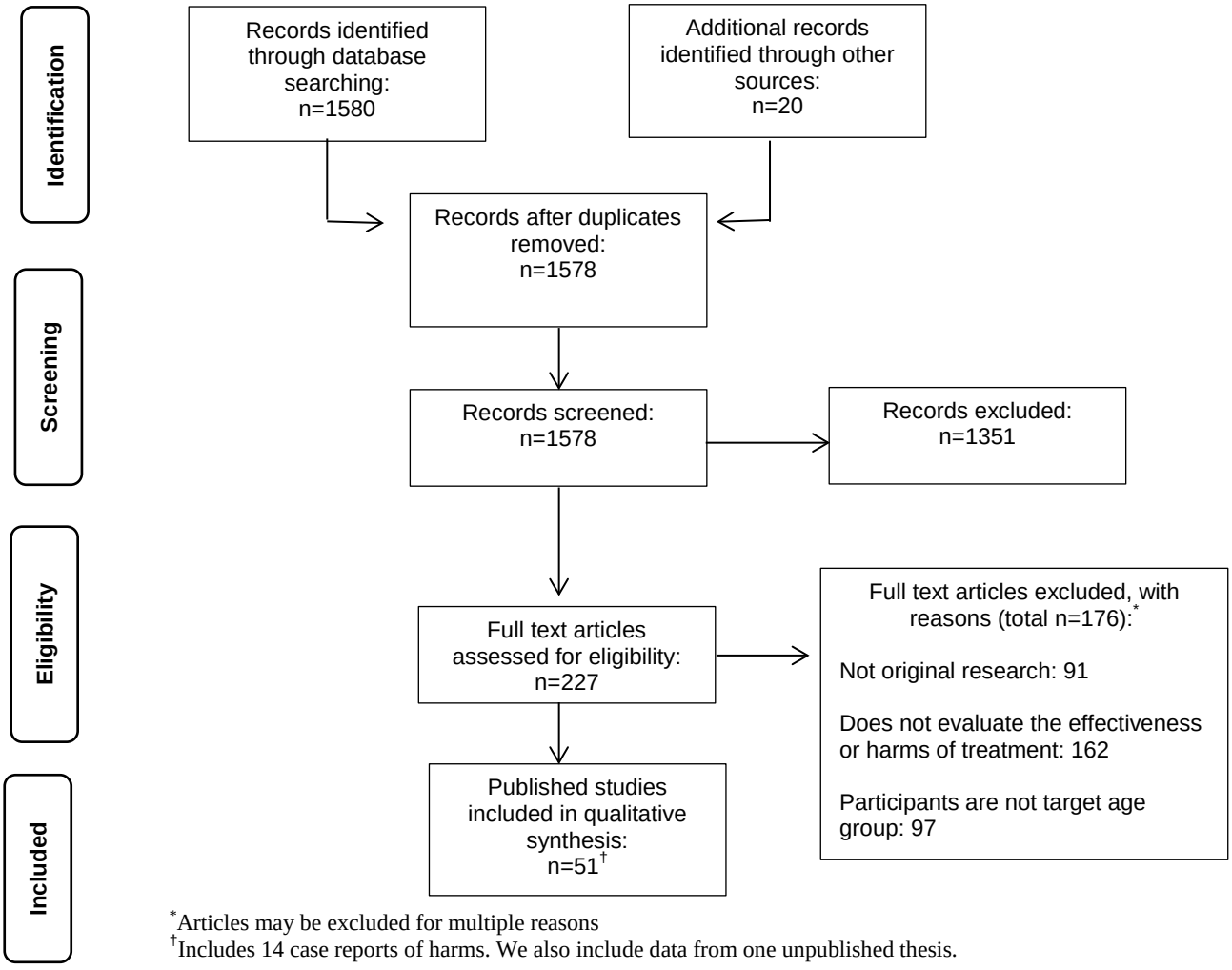
We assessed the applicability of findings reported in the included literature to the general population of children with ankyloglossia by determining the population, intervention, comparator, and setting in each study and developing an overview of these elements for each intervention category. We anticipated that areas in which applicability would be especially important to describe would include the severity of ankyloglossia in the study population, the age range of the participants, and the setting in which the intervention took place. We also attempted to capture information about the clinical provider including specialty and training. We describe any needs related to the setting, including anesthesia, surgical environment, materials for non-surgical interventions, etc.

Results

Results of Literature Searches

We identified 1578 nonduplicative titles or abstracts with potential relevance, with 227 proceeding to full text review (Figure 3). We excluded 176 studies at full text review, which yielded 51 published studies included in the review. We also included one unpublished thesis in our results, thus the report summarizes data from 52 unique publications.

Figure 3. Disposition of articles identified by the search strategy



*Articles may be excluded for multiple reasons
†Includes 14 case reports of harms. We also include data from one unpublished thesis.

Description of Included Studies

The 51 unique published studies included in the review comprise six randomized controlled trials (RCTs), three assessed as good quality[7, 8, 20] for outcomes related to breastfeeding effectiveness and maternal pain related to breastfeeding. One RCT was rated as poor quality for breastfeeding effectiveness and pain outcomes.[21] One RCT was of poor quality for outcomes of tongue protrusion, frenulum length, and articulation/intelligibility,[22] and we rated one RCT as

fair quality for measures of breast and bottle feeding.[23] The literature also includes three cohort studies (all poor quality[24-26]), 28 case series,[3, 6, 27-52] and 14 case reports (one of which reports two cases).[53-66] Table 6 outlines study characteristics.

Because case series do not include comparison groups, they do not provide comparative effectiveness data but were read to determine if they generally provided support for comparative data and as an additional source of harms. We used case reports to seek harms data only. We considered all comparative studies (RCTs and cohort studies) as poor quality for harms outcomes. We considered the quality for harms outcomes as good in four case series[49-52] and poor in 24.[3, 6, 27-48] We also include one unpublished thesis (not quality rated).

Table 6. Overview of comparative studies included

Characteristic	RCTs	Cohort Studies	Prospective Case Series	Retrospective Case Series	Total Literature
	(n=6)	(n=3)	(n=18)	(n=10)	(n=37)*
Intervention					
Frenotomy	3	3	2	4†	12†
Frenulotomy	0	0	5	1	6
Frenectomy	0	0	2	0	2
Frenuloplasty	0	0	3	2†	5†
Horizontal-to-vertical frenuloplasty	1††	0	0	0	1††
Four-flap Z-frenuloplasty	1††	0	0	0	1††
Z-plasty with partial myotomy	0	0	0	1	1
Laser excision	0	0	2	0	2
Tongue-tie division	2	0	4	3	9
Length of last followup					
Immediately after intervention	1	1	2	1	5
≤1 month	0	0	7	1	8
>1 to ≤3 months	2	0	5	2	9
>3 to ≤6 months	1	0	1	2	4
>6 to ≤12 months	1	0	0	0	1
>12 months	1	2	1	1	5
Not reported/unclear	0	0	2	3	5
Provider					
Family practitioner	0	0	1	0	1
Pediatrician	0	0	1	1	2
Otolaryngologist	1	2	3	2	8
Otolaryngologist consultant or lactation consultant	0	0	1	0	1
Lactation consultant or pediatric surgeon	2	0	0	1	3
Neonatologist or pediatric dentist	1	1	1	0	3
Surgeon	0	0	6	3	9
Not reported/unclear	2	0	5	3	10

Table 6. Overview of comparative studies included (continued)

Characteristic	RCTs	Cohort Studies	Prospective Case Series	Retrospective Case Series	Total Literature
Study population					
United States/Canada	2	2	5	3	12
Europe	3	0	7	4	14
Asia	0	0	1	2	3
Other	1	1	5	1	8
Total N participants	324	473	922	3821	5540

N=number; RCT=randomized controlled trial

* Literature also includes 14 case reports used for harms data and one unpublished thesis.

†One retrospective case series addressed frenotomy and frenuloplasty[48]

†† One RCT compared horizontal-to-vertical frenuloplasty to four-flap Z-frenuloplasty[22]

Key Question 1. Benefits of Interventions to Improve Breastfeeding Outcomes

Key Points

- Results for reduction in nipple pain immediately after surgery were inconsistent, and potentially associated with how early after birth surgery occurred, with the one good quality study with positive results including the youngest infants.
- Frenotomy was associated with significantly improved maternally reported breastfeeding effectiveness immediately post-procedure compared with sham in two RCTs[7, 20], but inconsistent evidence that it improved infant's latch and breastfeeding effectiveness compared with no intervention. Results on whether frenotomy prolonged duration of breastfeeding were unclear and not consistent.
- No comparative study identified expressly evaluated the role of non-surgical interventions in improving breastfeeding effectiveness.

Overview of the Literature

Twenty-five studies provided data on breastfeeding outcomes after surgical treatments for ankyloglossia. Only six included a comparison group and could provide information on comparative effectiveness. These studies included five randomized controlled trials conducted either in the United Kingdom (n=3),[8, 20, 23]United States (n=1),[7] or Israel (n=1)[21]and one retrospective cohort study conducted in the United States.[25] We rated three RCTs as good quality for outcomes related to breastfeeding effectiveness and pain related to breastfeeding.[7, 8, 20] One RCT was rated as fair[23] and one as poor quality for breastfeeding effectiveness and pain outcomes,[21] and we rated the cohort study as poor quality. The remainder of the studies were case series and therefore used to identify harms (n=19). Case series were conducted in the United Kingdom (n=9),[28, 29, 32, 35, 36, 39, 41, 49, 50]United States (n=4),[3, 31, 44, 45]Australia (n=3),[30, 38, 40]Finland (n=1),[48] Israel (n=1),[52] and Canada (n=1).[27]

In the studies that provided breastfeeding outcomes, ankyloglossia was only identified in the presence of breastfeeding difficulties. It was diagnosed by clinician examination in all

comparative studies but using different methods. In three studies, clinicians diagnosed it from exam without defining clear diagnostic criteria.[20, 23, 25] In others, ankyloglossia was defined as breastfeeding difficulties combined with either 1) Hazelbaker Assessment Tool of Lingual Frenulum Function (HATLFF) score between 6 and 12 and Latch, Audible swallowing, Type of nipple, Comfort, Hold (LATCH) score ≤8[8], or 2) abnormal HATLFF (cut-off not defined).[7]

Two RCTs compared frenotomy to sham surgery,[7, 20] one to usual care,[8] one to intensive lactation consultation,[23]and one used a crossover design to compare frenotomy followed by sham surgery to sham surgery followed by frenotomy with assessment of breastfeeding after each order of intervention (i.e., frenotomy and sham).[21] Similarly, the retrospective cohort study compared frenotomy to usual care.[25] The frenotomy procedure was explicitly described by three of five RCTs and the cohort study. In all descriptions, the frenulum was divided with straight scissors: straight iris (1),[25] blunt tipped (2),[20, 23] unspecified (1).[7] Two RCTs mentioned frenotomy without specifying how it was technically performed.[8, 21] The cohort study was the only comparative study that described systematic use of anesthetic (i.e., viscous lidocaine) prior to ankyloglossia division;[25] however, when case series were considered, a total of four of 25 studies reported use of some anesthetic before surgery.[3, 25, 31, 49]

Detailed Analysis

Overview by Study Design for All Breastfeeding Outcomes

Randomized Controlled Studies

Five RCTs addressed the benefits of treating ankyloglossia with frenotomy on breastfeeding outcomes among neonates and infants who had breastfeeding difficulties (Table 7). The first good quality RCT was single-blinded and randomly assigned infants causing maternally reported nipple pain or difficulty breastfeeding with concomitant and significant ankyloglossia diagnosed by lactation consultant based on HATLFF criteria to frenotomy (n=30) or a sham procedure (n=28).[7] Infants in this study were young (mean 6.0 ± 6.9 days), and had a gender distribution of approximately 2:1 male: female in both treatment groups. Primary outcomes were 1) nipple pain assessed using the Montreal Pain Questionnaire (MPQ-SF); 2) objective breastfeeding effectiveness using Infant Breastfeeding Assessment Tool (IBFAT); and 3) lingual frenulum function via the HATLFF appearance and function scores. Mothers assessed pain outcomes and were blinded to their infant's treatment group.

Mothers whose infants had frenotomy reported significantly less nipple pain immediately following the procedure (mean MQP-SF: 4.9 ± 1.46 vs. 13.5 ± 1.5, p<0.001), which remained significantly less than the sham group until the 4-week assessment. Moreover, the mean IBFAT score was higher among frenotomized infants than those undergoing the sham procedure (11.6 ± 0.81 vs. 8.07 ± 0.86, p=0.026) immediately post-procedure, but was no different from the sham group at 2-week postoperative evaluation.

A second good quality RCT randomized infants less than 4 months of age with breastfeeding problems and ankyloglossia to either frenotomy (n=30) or sham procedure (n=30). There was nearly identical distribution of males and females (~2:1) and mean ages between groups (33 vs. 28 days).[20] The primary outcome was objectively observed improvement in breastfeeding effectiveness using a score adapted from LATCH and IBFAT, and the secondary outcome was maternally reported improvement in breastfeeding immediately after intervention. Treatment allocation was blinded to both the parents and independent outcome assessor.

No difference in breastfeeding improvement was reported by trained objective observers immediately following intervention (50% [13/26] vs. 40% [12/30]). In contrast, mothers whose infants had frenotomy reported significantly improved breastfeeding compared with those in the sham group (78% [21/27] vs. 47% [14/30] $p<0.02$). There was no immediate difference in the reduction in maternal reported pain scores between the frenotomy and sham groups (mean -2.5 ± 1.9 and -1.3 ± 1.5, $p=0.13$). Although the study reports that they re-assessed outcomes at 3 months, the data are not provided by treatment group. A third good quality RCT randomized term infants with breastfeeding difficulties and ankyloglossia (HATLFF score between 6 – 12 and LATCH score ≤ 8) to either frenotomy (n=55) or no intervention (n=52).[8] All dyads consulted with a lactation consultant prior to randomization. Infants with severe ankyloglossia (defined as HATLFF < 6) were excluded and offered immediate frenotomy. At randomization, the median age was 11 days (IQR 8 – 14) and 11 days (IQR 8 – 16) in the frenotomy and control groups, respectively (p=0.94). This study did not report on gender of enrolled infants, but matched infants on age and birth order. Primary outcomes assessed 5-days and 8 weeks post-procedure included 1) change in maternal pain using VAS and 2) LATCH score. Secondary outcomes were method of feeding (i.e., bottle vs. breast), percent breastfeeding, and Breastfeeding Self-Efficacy Scale-Short Form (BSES-SF) score. Independent researchers collecting outcomes, but not mothers, were blinded to infant group assignment and performed assessment at the 5-day follow-up visit. The 8-week assessment was limited since 35 of 52 in the comparison group requested frenotomy before that follow-up date due to continued breastfeeding problems. Therefore, the 8-week comparison was between 52 of 55 of the frenotomized infants, and 50 of 52 in the "no intervention" group of whom only eight of 50 (15%) had not had frenotomy at the time of this follow-up assessment.

Five days after the procedure, reductions in pain scores were not significantly greater among mothers whose infants had a frenotomy (median -2 [IQR -3 to 0.4] vs. -1 [-13.5 to 1]). Of note, 17 percent randomized to usual care did not wait 5 days before getting a frenotomy due to painful breastfeeding. Similarly, no significant improvement in median maternal pain was reported 8 weeks post-procedure (median -2 [IQR -3 to -1] vs. -2 [-3.5 to -0.6], p=0.83). Infant outcomes showed no differential median improvement between frenotomy and control group at 5-days for LATCH score (median 1 [IQR 0 – 2] vs. 1 [0 – 2], p=0.52) or IBFAT score (median 0 [IQR -1.8 to 1.0] vs. 0 [IQR 0 – 1]), p=0.36).

In contrast, compared with controls, there was improvement in both median BSES-SF score (median 9 [IQR 1.8 – 12.3] vs. 1 [-4 to 7.5] p=0.0002) and HATLFF score (4.5 [IQR 3.3 – 6] vs. 0 [0 – 2.3], $p<0.001$) 5-days post-intervention in the frenotomy group. Between 5-days and 8 weeks post-intervention, there was less improvement in the median BSES-SF score among frenotomy infants compared with those in the control group, but this difference was not statistically significant (3 [IQR 0 – 13] vs. 10 [2 – 18], p=0.082). The BSES-SF improvement occurred more rapidly after frenotomy in the surgery group than in the control group, but by 8-weeks both groups were nearly equivalent in overall improvement (5-day median + 8-week median: frenotomy 9 + 3=12 vs. control 1 + 10=11). However, this comparison is difficult to interpret because so many control infants underwent frenotomy between the 5- and 8-week assessments. Crossover to frenotomy may also explain the equivalence of exclusive breastfeeding rates between groups at the 8-week assessment (intervention 82.7% vs. 80%, p=0.73).

A fair quality RCT randomized infants born with ankyloglossia diagnosed within the first 5 months with feeding problems to either frenotomy (n=28) or a control group who had intensive

support, advice and help from lactation consultants (n=29).[23] Degree of ankyloglossia was gauged by clinician visualization to be between 0 percent (i.e., none) and 100 percent (i.e., to the tongue tip). Tongue-tie length was 25 percent in six patients, 50 percent in 13, 75 percent in 15, and 100 percent in 23. Infants in both the frenotomy and control group had similar ages (20 vs. 18 days), but gender distribution was only recorded for the frenotomy group where there was a 1:1 ratio of males to females. The primary outcome was maternally reported improvement in breastfeeding. Most (96 percent) of frenotomized infants had improved feeding with 48 hours compared with 3 percent in the control group. The study was, however, entirely unblinded and all outcomes were by maternal report.

The final poor quality trial randomized full-term healthy for gestational age infants, ages 1 to 21 days, who were referred to a lactation clinic due to maternal nipple pain, and diagnosed with ankyloglossia by a neonatologist to either frenotomy followed by sham procedure (n=15) or vice versa (n=11) with assessment of breastfeeding after each intervention type in both arms.[21] Neither infant ages nor gender distribution was reported. The study's primary outcomes were maternal breastfeeding pain or nipple trauma measured by a standard Visual Analog Scale (VAS) and breastfeeding LATCH scores. Main outcome assessors were the mothers who were blinded to infant treatment group. Comparative group results were not reported, therefore preventing comparative analysis in this review.

Table 7. Breastfeeding effectiveness following surgical procedures

Study Study Design/Setting Groups, N Enrollment/ N Final Quality	Age in Days (IQR, Range, Mean, or Mean ± SD)	Baseline Measures	Outcomes at 5 Days	Outcomes at 8 Weeks
LATCH				
Emond et al. 2013[8] RCT/Hospital clinic G1: Frenotomy, 55/52 G2: Usual care, 52/50 Quality: Good	Mean at 5 days followup (IQR) G1: 11 (8-14) G2: 11 (8-16)	G1+G2: ≤ 8	Median (IQR) G1: 9 (8-10) G2: 9 (8-10) G1 vs. G2: p= 1.0	Median (IQR) G1: 10 (10-10) G2: 10 (10-10) G1 vs. G2: p= 0.41
Dollberg et al., 2006[21] RCT G1: Frenotomy, breastfeeding/ sham, breastfeeding, 15/14 G2: Sham, breastfeeding, frenotomy, breastfeeding, 11/11 Quality: Poor	Range of days G1+G2: 1-21	Mean ± SD G1+G2: 6.4±2.3	Mean ± SD G1+ G2: 6.8 ± 2.0 p=0.06 compared with baseline	NA
BSES-SF				
Emond et al. 2013[8] RCT/Hospital clinic G1: Frenotomy, 55/52 G2: Usual care, 52/50 Quality: Fair	Mean at 5 days followup (IQR) G1: 11 (8-14) G2: 11 (8-16)	NR	Median (IQR) G1: 54 (43-62) G2: 53 (40.8-61) G1 vs. G2: p= 0.53	Median (IQR) G1: 63 (59-68) G2: 63 (57-69) G1 vs. G2: p= 0.62
IBFAT				
Emond et al. 2013[8] RCT/Hospital clinic G1: Frenotomy, 55/52 G2: Usual care, 52/50 Quality: Good	Mean at 5 days follow=up (IQR) G1: 11 (8-14) G2: 11 (8-16)	NR	Median (IQR) G1: 12 (11-12) G2: 12 (11-12) G1 vs. G2: p= 0.76	Median (IQR) G1: 12 (12-12) G2: 12 (12-12) G1 vs. G2: p= 0.58
Buryk et al. 2011[7] RCT/Newborn nursery or clinic, otolaryngology clinic G1: Frenotomy, 30 G2: Sham procedure, 28 Quality: Good	Mean days ± SD at enrollment G1: 6.2±6.9 G2: 6.0±7.0	IBFAT, mean ± SE G1: 9.3±0.69 G2: 8.5±0.73	Immediately after procedure, mean ± SE G1: 11.6±0.81 G2: 8.07±0.86 G1 vs. G2, p=0.029 Effect size: 0.31	NA

Note: Not all RCTs reported these measures. BSES-SF=Breastfeeding Self-Efficacy Scale-Short Form; G=group; IBFAT=Infant Breastfeeding Assessment Tool; IQR=interquartile range; LATCH=Latch, Audible swallowing, Type of nipple, Comfort, Hold; N=number; NA=not applicable; SD=standard deviation; SE=standard error

Cohort Studies

A single poor quality retrospective cohort study compared frenotomy to no intervention.[25] It included 367 infants with feeding or latching difficulties that caused maternal pain when breastfeeding, 302 of whom underwent frenotomy. In this cohort, 58.6 percent of infants were male, mean age at ankyloglossia diagnosis was 18 days, and the majority of patients were either Caucasian (70.3%) or African American (15.5%). Ankyloglossia grade was recorded using Coryllos et al. system.[67] Overall, 17.4 percent had type I, 45.5 percent type II, 25.3 percent type III, 18 percent type IV, and 5.8 percent indeterminate. Outcomes were only assessed in the 91 mothers (24.9%) who agreed to participate in a follow-up survey (82 had frenotomy, 9 no intervention), thus limiting its generalizability. Nonetheless, 80.4 percent of interviewed mothers whose infant had undergone frenotomy felt it had benefited their child's ability to feed. Breastfeeding was continued in 82.9 percent of 82 frenotomized infants for a mean 7.09 months total compared with 66.7 percent of nine infants not treated who breastfed a mean 6.28 months total. In all, 17.1 percent and 33.3 percent in the frenotomy and no intervention group stopped breastfeeding due to difficulty or pain due to ankyloglossia. Having a frenotomy in the first week of life versus later did not affect the total months of breastfeeding (mean: ≤7 days 7.11 vs. >7 days 7.06 months; $p<0.9$).

Case Series

We identified 19 case series that addressed treatments for ankyloglossia on effectiveness of breastfeeding. All studies focused on surgical treatments, which included frenotomy, frenulotomy, or frenuloplasty. None explicitly evaluated non-surgical interventions. By design, none included a comparison group, thereby eliminating the ability to assess comparative effectiveness of surgical approaches, although the studies typically reported improvements in breastfeeding effectiveness after surgery. Harms reported in case series are included in KQ5, below.

Analysis of Breastfeeding Effectiveness

Immediate Outcomes

Breastfeeding effectiveness was evaluated in four of five RCTs (Table 8).[7, 8, 20, 23] We rated two RCTs as good quality for these outcomes[7, 20] and two as fair quality.[8, 23] Among the three RCTs that used a blinded independent reviewer to assess effectiveness,[7, 8, 20] one reported objective improvement in breastfeeding effectiveness based on IBFAT score immediately post-frenotomy compared with sham treatment (mean 11.6 ± 0.81 vs. 8.07 ± 0.86; $p=0.026$).[7] In contrast, in two of the three RCTs, the independent blinded observers did not detect a difference in breastfeeding improvement. Outcomes that failed to show a difference in these two RCTs included percent improvement (50% vs. 40%) immediately after intervention[20]and LATCH and IBFAT change 5-days post-intervention (LATCH change: median 1 [IQR 0 – 2] vs. median 1 [IQR 0 – 2], $p=0.52$ and IBFAT change: 0 [IQR -1.8 to 1.0] vs. 0 [IQR 0 – 1], $p=0.36$).[8]

Three of four RCTs with usable data used maternally reported improvement in breastfeeding as an outcome,[8, 20, 23] and in one, it was the primary outcome measure of effectiveness.[23] Maternally reported outcomes differed from objective independent assessment reported above. For example, in one RCT, mothers self-reported improved breastfeeding among infants immediately after frenotomy (78% in the treated group vs. 47% in the comparison group, $p<0.02$).[20] Similarly, another trial using non-blinded maternally assessed breastfeeding

effectiveness reported that 96 percent of frenotomized infants had improved feeding with 48 hours compared with 3 percent in a control group who had intensive lactation consultant support.[23] Finally, one RCT used the BSES-SF as a secondary outcome and found that mothers whose infants had had frenotomy had significantly improved scores 5 days after intervention (median BSES-SF =9 [IQR 1.8 – 12.3] vs. 1 [IQR -4 to 7.5], p=0.0002).[8]

Longer Term Outcomes

Three RCTs[7, 8, 20] and the retrospective cohort study[25] followed up dyads during the first postoperative year. One RCT contacted mothers 3 months after frenotomy, but did not stratify results by treatment group.[20] Overall, 92 percent (54/59) of all patients reported improved feeding, with 56 percent reporting full resolution of breastfeeding difficulties. Moreover, 65 percent (38/59) of infants were being breastfed at 3 months of age, whereas 51 percent (30/59) were continuing to breastfeed at second outcome assessment (4.5 months). The second RCT evaluated results 2-weeks post-operatively and found no difference between those who underwent frenotomy or sham treatment.[7] A third RCT found no difference in breastfeeding effectiveness between groups as measured by LATCH score at an 8-week follow-up survey, but mothers did report nonsignificantly improved BSES-SF scores among frenotomized infants.[8] Of note, 35 of 52 children assigned to the control arm had undergone frenotomy after 5 days. Seventeen of 35 had not had surgery, and two additional infants were lost to followup at 8 weeks.

The retrospective cohort reported that breastfeeding was continued in 82.9 percent of frenotomized infants for a mean 7.09 months total compared with 66.7 percent of infants not treated who breastfed a mean 6.28 months total. In all, 17.1 percent in the frenotomy and 33.3 percent in the no intervention group stopped breastfeeding due to difficulty or pain due to ankyloglossia. Having had frenotomy in the first week of life versus later did not affect the total months of breastfeeding (mean: ≤7 days 7.11 vs. >7 days 7.06 months; p<0.90).

Maternal Pain Outcomes

Among comparative studies, three RCTs, rated as good[7, 8, 20] for pain outcomes, reported on maternal nipple pain outcomes. Of these, one reported significant and immediate improvement in maternally reported nipple pain among mothers of frenotomized infants compared with sham treatment.[7] Both remaining RCTs found nonsignificant reductions in maternally reported nipple pain between the frenotomy and sham groups at immediate[20] and 5-day[8] post-procedure assessments. Of note, 17 percent of infants randomized to no intervention in the study that followed patients out five days[8] requested and received early frenotomy before the data were collected.

Table 8. Breastfeeding-associated pain scores after surgical procedures

Study Study Design/Setting Groups, N Enrollment/ N Final Quality	Age in Days	Baseline Measures, Mean ±SD	Followup Measures
Visual Analog Scale			
Emond et al. 2013[8] RCT/Hospital clinic G1: Frenotomy, 55/52 G2: Usual care, 52/50 Quality: Good	Mean at 5 days followup (IQR) G1: 11 (8-14) G2: 11 (8-16)	NR	5 days, median (IQR) G1: 3 (1-4.3) G2: 3 (2-6) G1 vs. G2: p=0.13 8 weeks, median (IQR) G1: 0 (0) G2: 0 (0-1) G1 vs. G2: p=0.41
Berry et al. 2012[20] RCT/Hospital (not specified) G1: tongue-tie division, 30/27 G2: sham procedure, 30/3 Quality: Good	Mean (range) G1: 33 (6-115) G2: 28 (5-111)	G1: 4.1± NR G2: 4.2± NR	Mean immediately after procedure G1: 1.6 G2: 2.9 Mean change ± SD: G1: -2.5 ± 1.9 G2: -1.3 ± 1.5, p=0.13 (95% CI: -0.3 to 2.4)
Short-Form McGill Pain Questionnaire			
Buryk et al. 2011[7] RCT/Newborn nursery or clinic, otolaryngology clinic G1: Frenotomy, 30 G2: Sham procedure, 28 Quality: Good	Mean ± SD at enrollment G1: 6.2±6.9 G2: 6.0±7.0	G1: 16.8±10.6 G2: 19.2±9.9	Mean ± SD immediately after procedure G1: 4.9±1.46 G2: 13.5±1.5 G1 vs. G2: p<0.001 Effect size: 0.38

G=group; IQR=interquartile range; N=number; NR=not reported; RCT=randomized controlled trial; SD=standard deviation

Key Question 2a. Benefits of Treatments to Mitigate Feeding Sequelae

Key Points

- Existing data are insufficient to draw conclusions about the benefits of surgical interventions for infants and children with ankyloglossia on medium- and long-term feeding outcomes other than breastfeeding. The studies used different populations and measured different outcomes.

Overview of the Literature

We identified three studies examining medium- and long-term benefits related to feeding outcomes and sequelae of various interventions for infants and children with ankyloglossia (Table 9).[23, 24, 35] One was an RCT[23] (fair quality for feeding outcomes) and one was a poor

quality retrospective cohort study[24]; the remaining study was a case series.[35] All studies were single center or single surgeon studies. Two studies were conducted in the United Kingdom[23, 35] and one study in the United States.[24]

Detailed Analysis

Comparative data were included in two studies.[23, 24] A detailed description of the included fair quality RCT study design and population are reported in the detailed analysis for Key Question 1. In summary, the study[23] randomized infants born with ankyloglossia and diagnosed within the first 5 months with feeding problems to either frenotomy (n=28) or a control group who had intensive support, advice and help from lactation consultants (n=29). Outcomes were based solely on maternal-report within 48-hours of randomization. However, in the RCT the control group was offered – and the majority elected to receive –frenotomy within 48 hours of randomization to the comparison group, so the outcomes do not reflect "medium to long term" feeding outcomes. This study was included herein, because it includes data on bottle-feeding efficiency. Outcomes related directly to breastfeeding are presented in Key Question 1.

Among pre-treatment bottle fed infants, 76 percent had major problems with dribbling, and 71 percent had "excess wind" (gas). Mothers reported significant improvement in feeding in all eight who received the frenotomy and in none who did not. The interval to ascertainment of outcomes was not specifically reported, but outcomes were obtained within the first 4 weeks of life.

The retrospective cohort study compared parent-reported (typically maternal) outcomes at age 3 years for children born in 2010 who 1) received frenotomy for tongue-tie (n=71; frenotomy group), 2) were offered but declined frenotomy for tongue-tie (n=15; no frenotomy group), and 3) children without ankyloglossia (n=18; control group).[24] Three questions rated on a 5-point Likert scale were used to assess a child's difficulty (a) cleaning his or her teeth with the tongue, (b) licking the outside of his or her lips, and (c) eating ice cream. With respect to answers on each of the questions, the frenotomy group performed better than the no frenotomy group at age 3 years and did not differ significantly from the comparison group without ankyloglossia. P-values were presented without reporting the central tendency (e.g., median, mean) or variance (IQR, SD) from which they were calculated. Therefore, further comparative description or analysis was not possible.

In the case series of 62 infants, 51 had complete outcome data (11 lost to follow-up).[35] Of these, infant ages ranged from 12 to 35 days at time of referral for frenulotomy by plastic surgeon, and outcomes were assessed prospectively over an 8-month period, on the day of frenulotomy, and at 2-weeks post-procedure at outpatient appointment. Over this period, the number of breastfeeding sessions decreased from 10 ± 0.7 pre-frenulotomy to 7 ± 0.5 post-frenulotomy ($p<0.0001$) and bottle feeding supplementary sessions per day were reduced from nine to two at 2-week follow-up ($p<0.0001$). The authors suggest that this reflects longer-term improvement in feeding efficiency.

Table 9. Feeding sequelae

Study Study Design/Setting Groups, N Enrollment/N Final Quality	Age, Mean Days	Outcomes
Hogan et al. 2005[23] RCT/Outpatient (not specified) G1: Tongue-tie division, 28/28 G2: Usual care and advice from lactation consultants, 29/29 Quality: Fair	G1: 20 G2: 18 Range G1+G2: 3-70	• 96% of G1 infants improved in overall (breast and bottle) feeding (as rated by mothers) compared with 3% in G2 (p<0.001) • Feeding improved in 100% (n=8) of bottle fed infants in G1 vs. 0 in G2 (p<0.001) • Most G2 participants also received frenotomy shortly after randomization
Walls et al. 2014[24] Retrospective Cohort/Outpatient clinic, postpartum ward G1: Frenotomy, 71/71 G2: No surgery, 15/15 G3: No ankyloglossia, 18/18 Quality: Poor	3 years	• More children in G1 vs. G2 improved in oral motor activities including difficulty cleaning teeth with tongue (p=0.0006), difficulty licking outside of lips (p<0.0001), and difficulty eating ice cream (p=0.0003) • Outcomes did not differ significantly between participants in G1 and G3

G=group; N=number; NR=not reported; RCT=randomized controlled trial

Key Question 2b. Benefits of Treatments to Prevent Other Sequelae

Key Points

- Two studies reported better articulation among children who had received ankyloglossia treatment compared to those who had not, but results related to word, sentence, and fluent speech were inconsistent.
- Results in two studies comparing children with ankyloglossia who received treatment to children without a history of ankyloglossia were inconsistent.
- One small, poor quality RCT compared two surgical methods and reported that children in a four-flap Z-frenuloplasty group had greater articulation gains than those in the horizontal-to-vertical frenuloplasty group.
- Although a number of case series report positive outcomes related to speech after treating ankyloglossia, most discussed modalities, with safety, feasibility or utility as the main outcome, rather than speech itself.

Overview of the Literature

Nine studies addressed ankyloglossia treatment in children with speech and articulation concerns. One RCT[22] rated as poor quality comparing two different surgical techniques and one poor quality cohort study[24] were conducted in the United States. An additional poor quality retrospective cohort study was conducted in Israel (Table 10).[26] Of six case series addressing this question, two were conducted in the United States,[42, 43] one each from the United Kingdom,[51]China,[37] India,[47] and Korea.[34] No study addressed the effect of ankyloglossia on sleep disordered breathing, dental/occlusal issues, or dysphagia.

Among the comparative studies identified, two of three had speech and articulation assessed by speech language pathologists,[22, 26] while the third relied on parental report.[24] Professional assessment was performed by speech language pathologists using a validated articulation test (Articulation and Naming Test)[26]in one of two studies in which they were the outcome assessors and with the other using consensus between speech therapists.[22] The third study used a non-validated parental survey to determine severity of the child's articulatory abnormalities.[24]

Detailed Analysis

Cohort Studies

One poor quality retrospective cohort study[24] compared three treatment groups of children who were three years old in 2010 who had: 1) ankyloglossia and frenotomy within the first month of life (n=71), 2) ankyloglossia and whose parents declined frenotomy during the same period (n=21), and 3) a control group of randomly selected 3-year old patients with no history of ankyloglossia (n=18). Three-year old subjects were chosen because that is the age that speech and articulation abnormalities typically present. Pediatric otolaryngologists determined the ankyloglossia severity using Coryllos criteria in the postpartum ward or during outpatient clinical examination. Parents of all identified patients were then contacted for a telephone survey that consisted of nine questions related to the healthcare provider who identified restriction, recommendations for surgery, intelligibility of speech to parent(s), impaired speech sounds, deficiencies in oral motor activities, and perceived need for speech therapy. Speech intelligibility was graded on a 5-point Likert scale (1=poor to 5=well-developed).

Overall, 36 of 86 with treated or untreated ankyloglossia had parent-identified speech difficulties. Three-way comparison found statistically improved speech scores among treated versus untreated groups (mean 4.52 ± 0.61 vs. 3.60 ±0.63, $p<0.0001$) and between the control and untreated groups (mean 4.33 ± 0.77 vs. 3.60 ±0.63, $p=0.01$). No difference was found between the treatment and non-ankyloglossia control arms. The authors suggest that these results indicate that frenotomy can improve speech, and that speech outcomes for children after frenulum release are on par with those of children who never had ankyloglossia. However, little information is provided about why children in the untreated group did not receive frenotomy or why certain children were treated.

A second poor quality retrospective cohort study recruited children who underwent frenotomy for ankyloglossia between ages of 2 days and 4 weeks and who were 4 to 8 years of age at the time of the study.[26] These children were age-matched to children with untreated ankyloglossia whose parents reported a history of breastfeeding difficulties (nipple pain and/or latching difficulties) and to children with no history of ankyloglossia. All patients were administered the Articulation and Naming Test[68] by two speech language pathologists who were

blinded to the group assignment. Each child's oral anatomy was systematically assessed from a standard oral motor evaluation test and scored.

In all, 23 children (17 males, 6 females) were divided into age-matched groups based on treatment status: treated (n=8; mean age 6.2 ± 1.8), untreated (n=7; mean age 6.2 ± 1.9), and controls (n=8; mean age 5.8 ± 1.9). All were found to have normal oral anatomy on examination. No significant differences were detected between treated and control patients in word, sentence, and fluent speech intelligibility. In contrast, children with untreated ankyloglossia had more articulatory errors than those who had been treated (14.5 ± 10 errors vs. 6.0 ± 4.2 errors).

Relevant case series examined different treatment methods including simple division with scalpel, scissors, and CO2 laser,[51] frenuloplasty,[42, 43] and the addition of genioglossus myotomy.[34] All studies reported positive outcomes and none reported significant harms, but as noted, these studies provide no comparative effectiveness data.

Table 10. Comparative studies with speech outcomes

Study **Study Design/Setting** **Groups, N Enrollment/ N Final** **Quality**	**Age in Years**	**Key Outcomes**
Walls et al. 2014[24] Retrospective cohort/Outpatient clinic, postpartum ward G1: Frenotomy, 71/71 G2: Untreated, 15/15 G3: No ankyloglossia, 18/18 Quality: Poor	3 years	• 36 of 86 patients in G1 and G2 were reported by parents to have speech difficulties at age 3 • Using a Likert scale of 1 (poor outcome), 3 (intelligible), 5 (well developed), parents reported (mean ± SD): G1: 4.52 ± 0.61 G2:3.60 ± 0.63 G3: 4.33 ± 0.77 • Parental measures of speech were significantly higher in G1 compared with G2 (p<0.0001) and G2 compared with G3 (p=0.01), but not in G1 compared with G3 (p=0.38)

Table 10. Comparative studies with speech outcomes (continued)

Study Study Design/Setting Groups, N Enrollment/ N Final Quality	Age in Years	Key Outcomes
Dollberg et al. 2011[26] Retrospective cohort/NR G1: Frenotomy, 8/8 G2: Untreated tongue-tie, 7/7 G3: No ankyloglossia, 8/8 Quality: Poor	G1: 6.2 ± 1.8 G2: 6.2 ± 1.9 G3: 5.8 ± 1.9	• Investigators assessed consonant articulation errors, word production accuracy, word intelligibility, sentence intelligibility and fluent-speech intelligibility. • Although differences were observed, including with treated children consistently having fewer problems across measures than untreated children, none of the differences was statistically significant, possibly due to small sample size. There were minimal, nonsignificant differences in the mean number of errors between treated children and those without ankyloglossia: Consonant articulation errors mean ± SD (SEM): G1: 6.0 ± 7.5 (2.7) G2: 7.1 ± 6.9 (2.6) G3: 1.0 ± 2.9 (1.0) G1 vs. G2: p=0.76 (95% CI: -6.96 to 9.19) G1 vs. G3: p=0.11 (95% CI: -1.43 to 11.39) Word production accuracy mean ± SD (SEM): G1: 6.0 ± 4.2 (1.5) G2: 14.5 ± 10.0 (3.7) G1 vs. G2: p=0.076 (95% CI: -1.15 to 18.09) G3: 8.8 ± 11.6 (3.1) G1 v. G3: p=0.53 (95% CI: -12.54 to 7.28) Word intelligibility mean ± SD (SEM): G1: 1.3 ± 0.1 (0.1) G2: 1.7 ± 0.36 (0.1) G1 vs. G2: p=0.33 (95% CI: 0.04 to 0.714) G3: 1.4 ± 0.4 (0.1) G1 vs. G3: 0.50 (95% CI: -0.46 to 0.25) Sentence intelligibility mean ± SD (SEM): G1: 1.3 ± 0.2 (0.1) G2: 1.6 ± 0.46 (0.2) G1 vs. G2: p=0.16 (95% CI: -0.147 to 0.749) G3: 1.4 ± 0.4 (0.1) G1 vs. G3: p=0.46 (95% CI: -0.49 to 0.24) Fluent-speech intelligibility mean ± SD (SEM): G1: 1.5 ± 0.4 (0.1) G2: 1.6 ± 0.5 (0.2) G1 vs. G2: p=0.6 (95%CI: -0.416 to 0.689) G3: 1.2 ± 0.3 (0.1) G1 vs. G3: p=0.229 (95%CI: -0.18 to 0.68)

CI=confidence interval; G=group; N=number; NR=not reported; SD= standard deviation; SEM=standard error of the mean

Comparison of Surgical Approaches

One RCT randomized children presenting to a cleft lip and palate-craniofacial clinic between 1999 and 2003 with a tight frenulum (<15 mm), an articulation or speech problem related to tongue tie, and/or age greater than 3 years to four-flap Z-frenuloplasty or horizontal-to-vertical frenuloplasty.[22] Technical aspects of both surgical procedures were well described. Primary outcomes were changes from pre-operative to follow-up (>10 months) in frenulum length, tongue-protrusion measurements, and speech assessment. Both frenulum length and tongue protrusion were measured pre- and post-operatively by trained independent raters. Each patient had speech evaluations performed by two independent speech pathologists.

The study included 16 children with articulation problems, of whom 11 underwent four-flap Z-frenuloplasty (7 male, 4 female) and the remainder (2 male, 3 females) horizontal-to-vertical frenuloplasty. Ages were similar between treatment groups (Z-frenuloplasty: mean 5.7 ± 2.14 vs. horizontal-to-vertical: mean 5.56 ± 1.52). Pre-operatively, children in the Z-frenuloplasty arm had articulation difficulties rated as severe in six (55%) and moderate in five by the speech pathologists. Of the five patients in the horizontal-to-vertical frenuloplasty group, three (60%) were rated as severe and two (40%) as moderate. Ten of eleven children in the Z-plasty arm had two orders of magnitude improvement (i.e., severe to mild) and seven had complete resolution of articulation problems. In contrast, no patients in the horizontal-to-vertical group had two order of magnitude improvement or complete resolution. Two had one level improvement in articulation and three had none. Table 11 reports key outcomes in comparative studies.

Table 11. Comparison of surgical approaches

Study **Study Design/Setting** **Groups, N Enrollment/ N Final** **Quality**	**Age in Years**	**Key Outcomes**
Heller et al. 2005[22] RCT/Craniofacial clinic G1: Four flap Z-frenuloplasty, 11/11 G2: Horizontal-to-vertical frenuloplasty, 5/5 Quality: Poor	G1: 5.7 ± 2.14 G2: 5.56 ± 1.52	• In the four-flap Z-frenuloplasty group, 6 (55%) participants were rated by a speech pathologist as having severe articulation difficulties at baseline; 4 (45%) were rated as having moderate difficulties. • After treatment, 10/11 had 2 orders magnitude improvement; 7 had complete resolution. • In the horizontal-to-vertical group, 3 (60%) participants were rated by a speech pathologist as having severe articulation difficulties at baseline; 2 (40%) were rated as having moderate difficulties. • After treatment, 2/5 had 1 order magnitude of improvement; 0 had complete resolution; 3 had no improvement

N=number; G=group; RCT=randomized controlled trial

Key Question 3. Benefits of Treatments to Prevent Social Concerns Related to Tongue Mobility

Key Points

- Evidence is insufficient to assess the effects of intervention on social concerns related to tongue mobility.
- Studies assessed different surgical interventions and different patient populations with widely varying age ranges.

Overview of the Literature

We identified nine studies that addressed either social concerns[24, 33, 42, 51] and/or tongue mobility.[6, 22, 26, 42, 43, 46, 51] Studies related to the effect of ankyloglossia on social concerns included one poor quality retrospective cohort[24] and three case series[33, 42, 51] that included outcome data for social concerns (e.g., drooling, embarrassment, kissing). The retrospective cohort was conducted in the United States[24] and case series in the United Kingdom,[51]United States,[42] and Brazil.[33] None reported objective measurements of social concerns; instead each used parent- or patient-report to measure improvement. Subject age ranges varied significantly with the cohort study concentrating on 3 year old children[24]and case series including wider age ranges.[33, 42, 51] The studies employed different surgical techniques and used different terminology without technical explanation: laser excision,[6, 51] frenotomy,[24, 33, 34] frenectomy,[6, 33] and horizontal-to-vertical frenuloplasty.[42, 43] Two studies described novel approaches to ankyloglossia repair, frenuloplasty with buccal mucosal graft,[46] and four flap Z-frenuloplasty.[22]

Studies assessing the effect of ankyloglossia treatment on tongue mobility included a single RCT from the United States (rated as poor quality for outcomes related to tongue mobility),[22]a poor quality retrospective cohort study[26] from Israel, and five case series: three from the United States[42, 43, 46] and one each from the United Kingdom,[51] and Brazil.[6] One of two comparative studies objectively measured frenulum length and tongue protrusion,[22] while the other used speech pathologists to rate children's tongue movement.[26]

Detailed Analysis

Social Concerns

One comparative study addressed the effect of ankyloglossia treatment on social concerns unrelated to speech.[24] This retrospective cohort study enrolled 3-year old patients who received a frenotomy in infancy (n =71) and age- matched children with untreated ankyloglossia (n=15) and a control group of children without ankyloglossia (n=18). This study design and patient population is described in detail in KQ2 as it relates to feeding outcomes and in KQ2b with respect to speech outcomes. In short, parents were contacted in a telephone survey developed by a speech pathologist using a Likert scale to detect improvement in 1) difficult cleaning teeth with tongue, 2) difficulty licking outside of lips, and 3) difficulty eating ice cream.

Compared with individuals with non-treated ankyloglossia, those that were treated had significantly less difficulty cleaning the teeth with the tongue ($p = 0.0006$), licking the outside of their lips ($p < 0.0001$) and eating ice cream ($p = 0.0003$). Similarly, control patients had significantly less difficulties with these tasks compared with untreated children ($p<0.05$). Unfortunately, the central tendency and variance from which these p-values were derived were

not presented in the manuscript. Because this study was retrospective and included only parent report, both recall bias and confounding by indication are likely.

In one case series of older patients (mean age 29.8 ± 10.0 years), pre- and post-procedure patient survey was used to determine improvement.[42] Seven of 15 participants reported embarrassment due to their ankyloglossia. In the six patients who elected to undergo frenuloplasty (mean age 17.3 ± 3.2 years), all reported improvement in tongue function in at least three of six areas which included: licking ice cream, licking lips, cleaning teeth, kissing, and playing a wind instrument. Another case series reported subjective improvement in oral hygiene (n=18/21) after laser frenectomy.[51] Limiting these findings was the absence of pre-procedure status of these patients in these domains and how each was assessed. In addition to not including a comparison group of any type, case series are strongly affected by selection bias and are, by nature, not comparative studies.

Tongue Mobility

We identified two comparative studies that provided data on tongue mobility (Table 12).[22, 26] One RCT enrolled 16 children (mean age 5.7±2.14) randomized to either four-flap Z-frenuloplasty or horizontal-to-vertical frenuloplasty.[22] A thorough review of its study design is described in KQ2b in relation to speech outcomes. Authors measured frenulum length and tongue protrusion using a string to record the distance from the lower dentition to tongue tip during maximum protrusion of the tongue. The string was then transferred to a ruler for measurement in millimeters (mm). Three trained raters measured each patient's tongue protrusion.

The study reported improved tongue tip mobility in all 11 patients who underwent Z-frenuloplasty. The mean frenulum length in this group was 49.4 ± 16.6mm, which was significantly longer than pre-operatively (11.9 ± 6.1 mm, $p<0.001$). Thus, the mean gain in length was 37.5 ± 13.5 mm. In contrast, mean frenulum length for horizontal-to-vertical frenuloplasty was 22.6 ± 7.02 from 11.4 ± 3.36 mm, which was significantly longer, but less so than in the comparison group. Both groups were able to protrude the tongue past the inferior dentition. Mean gains in tongue protrusion for Z-frenuloplasty and horizontal-to-vertical frenoplasty were 36.2 ± 7.6 mm and 13.2 ± 2.6 mm, respectively. Measurements in both groups were significantly improved from baseline (p values <0.01).

The retrospective cohort study compared outcomes among children with ankyloglossia that was treated with frenotomy (n=8), untreated children with ankyloglossia (n=7) and a control group without a history of ankyloglossia (n=8). Design of this cohort is summarized as part of KQ2b in relation to speech outcomes. In terms of tongue mobility, speech pathologists examined each child's oral anatomy and tongue movements by performing 10 different exercises as part of a standardized oral motor evaluation test: protrusion, elevation, left and right movements, licking of lower and upper lips, clicking, touching hard palate, elevation of mid-tongue toward the hard palate). Each task was scored from 0 (normal) to 1 (for distorted movement or inability to perform task). Untreated individuals had more difficulties in tasks of tongue movement (11.4 ± 7.6 uncompleted tasks) compared with treated children (3.7 ± 4.2). Children with no history of tongue-tie had the lowest rate of uncompleted tasks (1.2 ± 1.6).

Five case series reported improvements in mobility and elevation.[6, 42, 43, 46, 51] Two case series assessing the safety of CO2 laser (total n=36) concluded that it was safe and effective alternative to conventional release.[6, 51] Both studies reported improvement in tongue mobility after repair but one[6] described greater improvement if the patient received speech therapy prior to release. A

third case series in participants (mean age 8 at surgery, 15 with ankyloglossia and two with short labial frenulums) reported improvements in tongue mobility in the 3-4 months following surgery in an unspecified number of participants.[46] For most of these studies there was minimal explanation of expectations for normal tongue mobility. For the few studies with objective measurements, the total sample size (n= 52) was too small and the ages too varied to establish normative data.

Table 12. Outcomes of interventions for social concerns related to tongue mobility

Author, Year Study Design/Setting Groups, N at Enrollment/Followup Quality	Age, Years, Mean ± SD	Key Outcomes
Social Concerns		
Walls et al. 2014[24] Retrospective cohort/Outpatient clinic, postpartum ward G1: Frenotomy, 71/71 G2: Untreated, 15/15 G3: No ankyloglossia, 18/18 Quality: Poor	3	• More parents in G1 vs. G2 reported improvements in difficulty in cleaning teeth with tongue (p=0.0006), difficulty licking outside of lips (p<0.0001), and difficulty eating ice cream (p=0.0003) • No significant differences between G1 and G3
Tongue Mobility		
Heller et al. 2005[22] RCT/Craniofacial clinic G1: Four flap Z-frenuloplasty, 11/11 G2: Horizontal –to-vertical frenuloplasty, 5/5 Quality: Poor	G1: 5.7 ± 2.14 G2: 5.56 ± 1.52	• Mean frenulum length increased from mean 11.9 ± 6.1 mm to 49.4 ± 16.6 mm (p<.0001) in G1 and from 11.4 ± 3.36 mm to 22.6 ± 7.02 (p=0.02) in G2 • Mean gain in tongue protrusion of 36.2 ± 7.6 mm (range 23-45 mm) in G1 (p<.0001); mean gain for G2 was 13.2 ± 2.6 (range 9-16) mm (p=0.0003) • Study did not define optimal ranges for tongue mobility
Dollberg et al. 2011[26] Retrospective cohort/NR G1: Frenotomy, 8/8 G2: Untreated tongue-tie, 7/7 G3: No ankyloglossia, 8/8 Quality: Poor	G1: 6.2 ± 1.8 G2: 6.2 ± 1.9 G3: 5.8 ± 1.9	• Children in G2 had more difficulties in tasks of tongue movement compared with G1 (11.4 ± 7.6 uncompleted tasks in G2 vs. 3.7 ± 4.3 in G1, p=0.12, 95% CI: -0.26 to 0.18) • Differences between G1 and G3 were not significant

G=group; mm=millimeters; N=number; RCT=randomized controlled trial; SD=standard deviation

Key Question 4. Benefits of Simultaneously Treating Ankyloglossia and Concomitant Lip-Tie

We identified no studies that presented outcomes specifically for infants or children treated simultaneously for ankyloglossia and lip tie. One study reported that some of the participants also had lip-tie, but the outcomes were not presented separately for this subset.[31]

Key Question 5. Harms of Treatments for Ankyloglossia or Ankyloglossia with Concomitant Lip-tie in Neonates, Infants and Children up to Age 18

Key Points

- Most studies that reported harms information explicitly noted that no significant harms were observed (n=18) or reported minimal harms, most commonly self-limited bleeding.

Overview of the Literature

We identified 27 studies addressing harms. One RCT conducted in the United Kingdom reported minor harms of surgery and need for reoperation.[8] A single retrospective cohort study conducted in the United States reported harms (scarring).[25]. Eleven of 28 case series reported minor harms: four from the United States,[3, 31, 42, 46] three from the United Kingdom,[29, 49, 50] one from Brazil,[52] one from Australia,[38] one from Israel,[52]and one from China[37] Case reports were specifically included to address harms; details of the 14 case reports yielding harms data are in Appendix G.

Detailed Analysis

Data on harms were only available for studies of surgical interventions. Given the paucity of comparative data on this topic, we also sought case series and case reports to ensure that we captured possible evidence of harms associated with treatment. Of six RCTs, four reported that there were no harms, one was silent on the subject, and one study reported that 64 percent of participants had a small white patch at the base of the frenulum and four of 99 (4%) required a reoperation.[8] Among the three cohort studies, two reported that there were no harms. In the one cohort study that reported harms, eight of 302 (2.6%) participants had a recurrence due to scarring or incomplete clipping that required reoperation.[25] Harms were described in 11 of 28 case series. Minor bleeding occurred in six and infant distress/pain was described as affecting 2 of 36 infants (5.6%) in another.[49] Rates of reoperation ranged from 0.1 percent[37] to 27 percent[31], with a need for reoperation occurring in a total of five case series. One case series reported mild wound cicatrization following frenuloplasty involving use of buccal mucosa grafts.[46] Another case series reported no complications after CO2 laser excision, but in patient surveys two of 21 disagreed with the statement “no pain” and one of 21 disagreed with the statement “no blood.”[51]

To ensure that we did not miss potential harms of surgical intervention, we searched for case reports of harms and identified 14,[53-66] details of which are presented in Appendix G. Among 14 case reports (one of which reported two cases[53]), there were two cases of surgical site infection, three cases of reoperation and three reports of swelling. Only two cases, in Nigeria, sustained harms to the degree that they were hospitalized for bleeding; in these cases, the authors indicated that the procedure was done by inexperienced clinicians and that this likely accounted for the excessive bleeding.[55]

Grey Literature

Conference Abstracts

We searched for conference paper and poster abstracts from recent national and international societies and associations related to pediatrics, nursing, breastfeeding medicine, lactation, otolaryngology, dentistry, orthodontics, speech and hearing. Conference abstracts predominantly addressed prevalence of ankyloglossia, investigation into incidence of anterior versus posterior rates of tongue-tie, rates of surgical treatment interventions, and case reports of successful surgical interventions to address breastfeeding issues. Results reported in abstracts generally aligned with our findings, with abstracts noting maternally reported improvements in breastfeeding effectiveness and nipple pain (Appendix H).

Dissertations and Theses

Although we did not identify any relevant dissertations in our search, one TEP member who recently completed a master's degree at the University of Liverpool allowed us to use findings from her unpublished thesis. She conducted a retrospective survey of parents in the United States of children who had had frenotomy for ankyloglossia either before or after age 12 weeks (Table 13).[69] The survey included questions related to breastfeeding effectiveness and pain, supplemental bottle feeding, feeding with solid food, knowing and pronouncing words, and oral hygiene and was sent to parents of children treated between 2006 and 2011 at a single institution. Findings supported the published literature in reporting improvements after frenotomy in maternally reported outcomes. This study adds to the published literature in assessing early versus late outcomes, finding improved outcomes associated with early treatment. Because it is not a published study, we did not include it in our strength of evidence assessment but provide the results here.

Findings included data from 125 children with ankyloglossia, 51 of whom were treated before 12 weeks of age (early treatment) and 74 who were treated after (late treatment). All children in the early treatment group were diagnosed within 90 days of birth, while 43 of the late treatment arm were diagnosed by 90 days, eight by 180 to 365 days, and 15 at >365 days of age.

Breastfeeding Outcomes

Children in the early treatment group had a longer duration of breastfeeding compared with the later treatment group, and infants in the early vs. late treatment group had a significantly greater likelihood of 1) problematic latch and resolution of the problem with frenotomy (45.1% vs. 1.4%, p=0.001), 2) maternal pain and resolution with frenotomy (33.3% vs. 1.4%, p=.001), 3) breastfeeding in a reasonable amount of time and resolution with frenotomy (34.7% vs. 0%, p=0.001). Children did not differ between groups on likelihood of issues of weight gain resolved by frenotomy. The need for supplemental bottle feeds resolved with frenotomy in four of five infants who required them in the early treatment group vs. in none of five children in the late treatment arm.

Other Feeding Outcomes

Twelve children in the early and nine in the late treatment group had issues with latch to a bottle that resolved with frenotomy in 100 percent of the early treatment group and 9.6 percent of the late treatment group. Infants in the early frenotomy group had significantly greater problems

latching; these infants also had higher rates of resolution than infants whose frenotomy occurred later. (p=0.045).

One child in the early group and four in the late had issues with spoon feeding that resolved with frenotomy in no early treated children and in 100 percent of late treated children. One early treated child had issues with solid foods that did not resolve with frenotomy while six late treated children had solid food issues, which resolved in 100 percent after treatment. Likelihood of issues with spoon feeding and resolution with frenotomy did not differ significantly between groups, while children in the late frenotomy group vs. early treated children had a greater likelihood of issues with solid food that resolved with frenotomy (p=0.035).

Speech Outcomes

No children in the early group and 40 in the late treatment group had issues with speech development. Issues resolved with frenotomy in 43.1 percent of the late treatment arm. Children with late frenotomy had a significantly greater likelihood of speech development issues that resolved with frenotomy compared with the early frenotomy group (p=0.01).

Other Outcomes

In this study, zero children in the early frenotomy group had oral hygiene issues, compared to 15 in late treatment arm. Issues resolved with frenotomy in 18.1 percent of children. Children in the late treatment group had a significantly greater likelihood of issues with oral hygiene that resolved with frenotomy than the early frenotomy arm (p=0.001).

Table 13. Outcomes reported in unpublished thesis*

Outcome	Issues with:	Not Breastfed or not an Issue or Issue Resolved Without Frenotomy N (% of Group)	Issue Resolved With Frenotomy N (% of Group)	Issue Did Not Resolve With Frenotomy N (% of Group)	Issue Resulted in Abandoning Breastfeeding N (% of Group)
Breast-feeding	**Latch to mother's nipple**				
	Early group	16/51 (31.4)	23/51 (45.1)		12/51 (23.5)
	Late group	61/74 (82.4)	1/74 (1.4)		12/74 (16.2)
	All	77/125 (61.6)	24/125 (19.2)		24/125 (19.2)
	Issues with maternal pain				
	Early group	27/51 (52.9)	17/51 (33.3)		7/51 (13.7)
	Late group	65/73 (89.0)	1/73 (1.4)		7/73 (9.6)
	All	92/124 (74.2)	18/124 (14.5)		14/124 (11.3)
	Breastfeeding in reasonable amount of time				
	Early group	22/49 (44.9)	17/49 (34.7)		10/49 (20.4)
	Late group	60/73 (82.2)	0/73 (0)		13/73 (17.8)
	All	82/122 (67.2)	17/122 (13.9)		23/122 (18.9)
	Supplemental bottle feeds				
	Early group	46/51 (90.2)	4/51 (7.8)		1/51 (2.0)
	Late group	69/74 (93.2)	0/74 (0)		5/74 (6.8)
	All	115/125 (92)	4/125 (3.2)		6/125(4.8)

Table 13. Outcomes reported in unpublished thesis* (continued)

Outcome	Issues with:	Not Breastfed or not an Issue or Issue Resolved Without Frenotomy N (% of Group)	Issue Resolved With Frenotomy N (% of Group)	Issue Did Not Resolve With Frenotomy N (% of Group)	Issue Resulted in Abandoning Breastfeeding N (% of Group)
Other Feeding Outcomes	**Latch to bottle**				
	Early group	37/49 (75.5)	12/49 (24.4)	0/49 (0)	
	Late group	64/73 (87.7)	7/73 (9.6)	2/73 (2.7)	
	All	101/122 (82.8)	19/122 (15.6)	2/122 (1.6)	
	Spoon feeding				
	Early group	50/51 (98)	0/51 (0)	1/51 (2)	
	Late group	69/73 (94.5)	4/73 (5.5)	0/73 (0)	
	All	119/124 (96)	4/124 (3.2)	1/124 (0.8)	
	Solid feeding				
	Early group	49/50 (98)	0/50 (0)	1/50 (2)	
	Late group	68/74 (91.9)	6/74 (8.1)	0/74 (0)	
	All	117/124 (94.4)	6/124 (4.8)	1/124 (0.8)	
Speech and Other Outcomes	**Pronunciation**				
	Early group	48/48 (100)	0/48 (0)	0/48 (0)	
	Late group	32/72 (44.4)	31/72 (43.1)	9/72 (12.5)	
	All	80/120 (66.7)	31/120 (25.8)	9 /120 (7.5)	
	Oral hygiene				
	Early group	50/50 (100)	0/50 (0)	0/50 (0)	
	Late group	57/72 (79.2)	13/72 (18.1)	2/72 (2.8)	
	All	107/122 (87.7)	13/122 (10.7)	2/122 (1.6)	

*Data reproduced with permission of Amanda Dale Tylor, MD, MPH
N=number

Discussion

We identified 51 published studies for this review, six of which were randomized controlled trials (RCTs), three were cohort studies, and the remainder case series (n=28) and case reports (n=14). The analysis and discussion concentrate on comparative studies (RCTs and cohorts), as these studies were used for strength of evidence assessment. Case series studies were included in the results only to ensure that the full range of available literature is made available to the end users of this report. Harms were reported from all included studies as well as a specific search for case reports.

Three RCTs were assessed as good[7, 8, 20] and one as fair[23] quality for outcomes related to breastfeeding effectiveness and associated maternal pain. One RCT was rated as poor quality for breastfeeding effectiveness and pain outcomes.[21] One RCT addressing tongue protrusion, frenulum length, and speech outcomes was rated as poor quality for those outcomes,[22] and we rated one RCT as fair quality for measures of bottle feeding.[23] We rated all three cohort studies as poor quality.[24-26]

We assessed the quality of harms reporting in RCTs and cohort studies as poor and as good in four case series[49-52] and poor in 24.[3, 6, 27-48] We also include data from one unpublished thesis (not quality scored).

Key Findings and Strength of Evidence

KQ1. Benefits of Interventions Intended to Improve Breastfeeding Outcomes

Key Findings

Overall, three good[7, 8, 20] and one fair[23] quality RCTs assessed whether treatment of ankyloglossia improved breastfeeding effectiveness. While only one of three RCTs that used blinded independent observers found significantly improved breastfeeding effectiveness among frenotomized infants immediately post-procedure,[7] maternally reported breastfeeding effectiveness was significantly improved in the treated group compared with untreated in two of two RCTs that evaluated it either as a primary[23] or secondary[20] outcome. A third RCT evaluated the mother's breastfeeding self-efficacy and found a significant improvement from baseline in the frenotomy group 5-days post-procedure.[8] In all, there is some evidence that maternally reported breastfeeding outcomes improve. Data are lacking to assess the durability of effects.

These same studies had disparate findings about whether frenotomy decreased maternal nipple pain during breastfeeding. Only the RCT performed on infants at 6 days of age showed a significant reduction in maternal pain.[7] Those performed on infants a few weeks older did not report either an immediate[20] or 5-day[8] reduction in pain. The difference between earlier frenotomy and later frenotomy on nipple pain may relate to cumulative trauma on the breast from several additional weeks with inefficient latch from tongue-tied infants.

Strength of the Evidence

Few comparative studies have addressed the effectiveness of surgical interventions to improve breastfeeding outcomes. Mothers consistently reported improved breastfeeding effectiveness, but outcome measures were heterogeneous and very short term. Future studies

could provide additional data to confirm or change the measure of effectiveness; thus we consider the strength of the evidence (confidence in the estimate of effect) to be low at this time.

We also considered the strength of the evidence to be low for an immediate reduction in nipple pain. Improvements were reported in the current studies, but additional studies are needed to confirm and support these results. Only one poor quality cohort study addressed effects on the length of breastfeeding; thus, we considered the strength of the evidence to be insufficient (Table 14).

Table 14. Strength of the evidence for studies addressing surgical approaches for ankyloglossia and breastfeeding outcomes

Outcome Number of Studies and Quality (Total Participants)	Study Limitations	Consistency	Directness	Precision	Reporting Bias	Finding/Strength of the Evidence
Nipple pain RCT: 3 good,[7, 8, 20] 1 poor[21] (251) Retrospective cohort: 1 poor[25] (367)	Low	Inconsistent	Direct	Imprecise	Undetected	Low SOE for an immediate reduction in nipple pain post-procedure due to inconsistent results across small studies.
Breastfeeding effectiveness RCTs-LATCH: 2 good,[8, 20] 1 poor [21] (193) IBFAT: 1 good[7] (58) BSES: 1 fair[8] (107) Retrospective cohort: 1 poor[25] (367)	Low	Inconsistent	Direct	Imprecise	Undetected	Low SOE for improved breastfeeding. Mothers consistently reported improved breastfeeding effectiveness, but outcome measures were heterogeneous and very short term. Observer-rated measures did not show effectiveness. Future studies could provide additional data to confirm or change the measure of effectiveness.
Length of breastfeeding Retrospective cohort: 1 poor[25] (367)	High	NA	Direct	Imprecise	Undetected	Insufficient SOE due to the high risk of bias of the one retrospective study

BSES=Breastfeeding Self-Efficacy Score; IBFAT=Infant Breastfeeding Assessment Tool; LATCH=Latch, Audible swallowing, Type of nipple, Comfort, Hold; NA=not applicable; RCT=randomized controlled trial; SOE=strength of the evidence

KQ2a. Benefits of Treatments to Mitigate Feeding Sequelae

Key Findings

We identified three studies examining feeding outcomes other than breastfeeding: one RCT,[23] one poor quality retrospective cohort study,[24] and one case series.[35] All three studies

were single center or single surgeon studies. Bottle feeding and ability to use the tongue to eat ice cream and clean the mouth improved more in treatment groups in comparative studies. Supplementary bottle feedings decreased over time in the case series.

Strength of the Evidence

With only two comparative studies, both with significant study limitations, existing data are insufficient to draw conclusions about the benefits of surgical interventions for infants and children with ankyloglossia on medium- and long-term feeding outcomes. The studies used different populations and measured different outcomes (Table 15).

Table 15. Strength of the evidence for studies addressing surgical approaches and feeding outcomes

Outcome Number of Studies and Quality (Total Participants)	Study Limitations	Consistency	Directness	Precision	Reporting Bias	Finding/Strength of the Evidence
Feeding outcomes RCT: 1 poor[23](57) Retrospective cohort: 1 poor [24](104)	High	Consistent	Indirect	Imprecise	Undetected	Insufficient SOE for all feeding outcomes given small number of participants, lack of standard outcome measures, and poor quality of studies.

RCT=randomized controlled trial; SOE=strength of the evidence

KQ2b. Benefits of Treatments to Prevent Other Sequelae

Key Findings

Speech concerns were the second most prevalent topic in the ankyloglossia literature, after breastfeeding. A speech language pathologist measured speech outcomes in two studies[22, 26] with the third using parental assessment.[24] No studies included data related to sleep disordered breathing, occlusal issues and dysphagia in the non-breastfeeding child. Two cohort studies attempted to assess the effectiveness of frenotomy, [24, 26] and one compared two surgical approaches to frenotomy. [22]

Two poor quality cohort studies[24, 26] reported an improvement in articulation and intelligibility with ankyloglossia treatment, but benefits in word, sentence and fluent speech were unclear. The one poor quality RCT reported improved articulation in patients treated with Z-frenuloplasty compared to horizontal-to-vertical frenuloplasty.[22] Numerous non-comparative studies reported a speech benefit after treating ankyloglossia; however these studies primarily discussed modalities, with safety, feasibility or utility as the main outcome, rather than speech itself.[33, 34, 37, 42, 43, 47, 48, 51]

Strength of the Evidence

Given the lack of good quality studies and limitations in the measurement of outcomes, we considered the strength of the evidence for the effect of surgical interventions to improve speech and articulation to be insufficient (Table 16).

Table 16. Strength of the evidence for studies addressing surgical approaches and other outcomes

Outcome Number of Studies and Quality (Total Participants)	Study Limitations	Consistency	Directness	Precision	Reporting Bias	Finding/SOE
Speech and articulation Retrospective cohort: 1 poor[24] (104) Prospective cohort: 1 poor[26] (23)	High	Inconsistent	Indirect	Imprecise	Undetected	Insufficient SOE based on 2 poor quality cohort studies
Oral motor skills Retrospective cohort: 1 poor [24](104) Prospective cohort: 1 poor[26] (23)	High	Consistent	Indirect	Imprecise	Undetected	Insufficient SOE based on 2 poor quality cohort studies

SOE-strength of the evidence

KQ3. Benefits of Treatments to Prevent Social Concerns Related to Tongue Mobility

Key Findings

Only one poor quality comparative, retrospective cohort study assessed outcomes related to social concerns other than speech.[24] It reported significantly improved ability to clean teeth with tongue, licking outside of lips, and eating ice cream in the treatment group compared with untreated participants. The intermediate outcome of improved tongue movement or mobility after ankyloglossia repair was assessed in two comparative studies—one poor quality RCT[22] and one poor quality cohort study.[26] The RCT assessed tongue mobility using two different surgical techniques for treating ankyloglossia and found that both approaches significantly improved tongue mobility, but that Z-frenuloplasty was superior.[22] In the cohort study, individuals with untreated ankyloglossia had the worst tongue mobility followed in order by children with treated ankyloglossia, and those with no history of ankyloglossia.[26]

Strength of the Evidence

With only one poor quality comparative study, strength of the evidence related to the ability of treatment for ankyloglossia to alleviate social concerns is currently insufficient. Also, with only three comparative studies with small sizes and limitations in the measurement of outcomes related to tongue mobility, we considered the strength of the evidence for the effect of surgical interventions to improve the short-term outcome of mobility to be insufficient (Table 17).

Table 17. Strength of the evidence for studies addressing surgical approaches social concerns related to tongue mobility

Outcome Number of Studies and Quality (Total Participants)	Study Limitations	Consistency	Directness	Precision	Reporting Bias	Finding/SOE
Social concerns Retrospective cohort: 1 poor[24] (104)	High	NA	Indirect	Imprecise	Undetected	Insufficient SOE based on 1 poor quality cohort study
Tongue mobility RCT: 1 poor[22](16) Retrospective cohort: 1 poor[26] (15)	High	Consistent	Direct	Imprecise	Undetected	Insufficient SOE based on 2 small, poor quality studies

RCT=randomized controlled trial; NA=not applicable; SOE=strength of the evidence

KQ4. Benefits of Simultaneously Treating Ankyloglossia and Lip-Tie

We did not identify any studies addressing this question.

KQ5. What are the Harms of Treatments for Ankyloglossia or Ankyloglossia with Concomitant Lip-tie in Neonates, Infants and Children up to Age 18?

Key Findings

We identified all possible harms reported within comparative studies and case series that potentially provided effectiveness data. We also sought case reports of harms. With this approach, we looked for harms in 49 studies that reported that they had looked for harms, either reporting actual harms or specifically indicating that they found none. These included six RCTs, one cohort study, 28 case series, and 14 case reports. We considered all comparative studies (RCTs and cohort studies) as poor quality for harms outcomes. We considered the quality for harms outcomes as good in four case series[49-52] and poor in 24.[3, 6, 27-48]Most studies that reported harms information explicitly noted that no significant harms were observed (n=18) or reported minimal harms. Among studies reporting harms, bleeding and the need for reoperation were most frequently reported. Bleeding was typically described as minor and limited. Few studies described what specific methods they used to collect harms data.

Strength of the Evidence

We considered the strength of the evidence for minimal and short-lived bleeding as a harm of surgical interventions as moderate based on an expanded search for harms reports in addition

to the comparative data. We considered the strength of the evidence for reoperation and pain as harms to be insufficient given the small number of studies that included these outcomes (Table 18).

Table 18. Strength of the evidence for studies addressing harms of surgical approaches

Outcome ***Number of Studies and Quality (Total Participants)***	Study Limitations	Consistency	Directness	Precision	Reporting Bias	Finding/SOE
Bleeding RCT: 1 poor[20] (60) Case series: 14 poor[6, 27-29, 32, 34, 35, 38-40, 42-45], 2 good [50, 51] (963)	High	Consistent	Direct	Imprecise	Suspected	Moderate SOE for minimal and short-lived bleeding based on an extensive search for harms reports in addition to the comparative data. Studies consistently reported minimal to no bleeding.
Reoperation RCT: 1 poor[8] (107) Retrospective cohort: 1 poor[25] (367) Case series:1 good,[50] 4 poor[3, 31, 37, 48] (3577)	High	Consistent	Direct	Imprecise	Suspected	Insufficient SOE due to very small numbers of the outcome reported at all in studies.
Pain Case series: 2 good[49, 51] (84)	High	Consistent	Indirect	Imprecise	Suspected	Insufficient SOE for minimal, short-lived pain in infants. No studies reported excessive crying or an inability to feed soon after the intervention, but pain is arguably difficult to assess in infants, so outcomes were indirect and from poor quality or noncomparative studies.

RCT=randomized controlled trial; SOE=strength of the evidence

Findings in Relationship to What is Already Known

Few recent reviews assessed outcomes of ankyloglossia treatment,[2, 5, 70] and our findings generally align with those prior reviews, concluding that current evidence is drawn from a small literature base with inconsistent findings related to the benefits of ankyloglossia treatments for increasing breastfeeding effectiveness or reducing maternally reported nipple pain. In a review focused solely on frenotomy and breastfeeding, the authors rated most of the seven studies evaluating frenotomy as poor quality (mean score of 24.4, range 9-40 on a 47-point scale).[70]

Studies included one RCT, and all used different outcome-measures to assess effects of frenotomy. Outcomes (breastfeeding mechanics, nipple pain, rate of breastfeeding, sucking, weight gain) all improved post-procedure, and no studies reported significant adverse effects. In a 2009 review addressing diagnosis and treatment and including 10 studies assessing effects of treatment on breastfeeding outcomes, breastfeeding mechanics and related outcomes typically improved.[2] Four studies of tongue mobility and three of speech problems also reported improvement. The review notes insufficient evidence related to choice of procedure, timing of procedure, or surgical versus conservative management; however, the investigators did not include any quality metrics for included studies.

The most recent systematic review, published in 2013, assessed outcomes related to breastfeeding and speech.[5] The 20 studies included ranged from level 4 case series to randomized controlled trials, and concluded that there is both objective and subjective evidence that frenotomy benefits breastfeeding (facilitated breastfeeding, enhanced milk transfer to the infant, and contributed to protecting maternal nipple and breast health), but tempered this by recognizing that there were a limited number of studies available with high quality evidence. Outcomes in four studies addressing speech articulation reported few definitive improvements following treatment. This review did not evaluate non-surgical management or broader outcomes.

Applicability

We set inclusion criteria intended to identify studies with applicability to newborns, infants, and children with ankyloglossia. Studies differed in terms of study population and outcome measures. Most studies were non-comparative, and lack of direct comparisons of treatment options further hinders the ability to understand what findings will best extrapolate to a specific newborn or infant or decisions about care protocols. Overall the data on breastfeeding and maternal breast pain that are available may be applicable to newborns with ankyloglossia with concomitant feeding problems. There is no evidence to suggest that the data would be applicable to infants with ankyloglossia who do not present with feeding problems. Appendix I contains applicability tables for individual key questions.

Applicability of Studies with Breastfeeding Outcomes

Newborns referred for treatment of ankyloglossia were born primarily at tertiary care centers and recognized as having difficulty with breastfeeding concomitant with ankyloglossia. Most infants are not born at tertiary care centers; thus extrapolation to other birthing sites may not be possible. Moreover, newborns of mothers not choosing to breastfeed may not be recognized as having and/or diagnosed with ankyloglosssia as breastfeeding difficulties were used as an indicator to evaluate for ankyloglossia. Interestingly, two studies[7, 8] reported that all patients had lactation consultation prior to enrollment without significant improvement in feeding. Arguably, this limits the applicability of their results to newborns that had failed to improve adequately with such consultation.

In these studies, various clinicians were involved in making the ankyloglossia diagnoses; however, assessment of breastfeeding difficulty and diagnostic criteria for ankyloglossia were not universally described. Lack of a consistent objective measure to define and classify this condition may limit the reproducibility of findings. Furthermore, patients in these studies were between a median 6 days of age[7] and up to a mean 33 days of age (range 6 to 115) in another

study.[20] Applicability to findings in older infants cannot be gleaned from this data; nor can durability of results.

Frenotomy was the only intervention employed in the good quality RCTs.[7, 8, 20] However, the specifics of the procedure were variably reported. As such the degree of posterior extension of the frenulum incision was not clearly defined and appears to be at the discretion and clinical expertise of the clinician. Also, the severity of the ankyloglossia was inconsistently reported, making inter-study generalizations difficult and, more importantly, limiting the broader applicability of findings.

The comparators used were sham surgery[7, 20] and usual care.[8] These outcomes are identical except in regards to blinding and outcome assessment. Both no intervention and sham surgery are perhaps misnomers, however, since these infant-mother dyads underwent usual care, which could include, but is not limited to, lactation consultation, supportive care, and bottle-feeding advice. Finally, there is insufficient evidence from available literature to assess the applicability of frenotomy on durability of breastfeeding. In other words, no conclusion could be made that tongue-tie division increases the duration of breastfeeding.

Applicability of Studies with Other Feeding Outcomes

Only one study with comparative poor quality retrospective cohort data addressed other feeding outcomes.[24] The study's intervention group received frenotomy for ankyloglossia, which was identified within the first month of life, and was compared to dyads who were also offered, but declined, frenotomy for the same indication in the same time period. Although this is a common decisional dilemma for parents of infants with congenital ankyloglossia, in usual clinical care, surgical intervention is not considered unless congenital ankyloglossia co-occurs with breast- or other feeding problems. Furthermore, there are several biases inherent in this treatment decision. First, those with "worse" ankyloglossia are more likely to get treated. Second, mothers who more strongly want to breastfeed may opt for division. Mothers who would rather pump or bottle feed with formula would more likely chose observation. Third, practitioners' presentation of the evidence may sway the decision, thus perpetuating their personal bias about effectiveness of frenotomy on improving breastfeeding and reducing maternal pain. Additionally, the study was conducted in an academic medical center in large, urban area with ankyloglossia severity graded by pediatric otolaryngologists. Therefore, applicability of its findings and observations may not translate to other care environments (i.e. community hospital, rural) and many usual clinical care settings may not include practitioners from this sub-specialty, instead relying more on pediatricians, lactation consultants, family practitioners, or dentists.

Applicability of Studies with Speech Outcomes

Comparative studies providing data on speech outcomes were all rated as poor quality and included a randomized controlled trial[22] and two retrospective cohort studies.[24, 26] The RCT compared two different frenuloplasty approaches for treatment of children of a mean age of approximately 6 years with a tight frenulum effecting articulation or intelligibility[22] and found that children treated with either four-flap Z-frenuloplasty and horizontal-to-vertical frenuloplasty had significant improvement in articulation as judged by trained speech language pathologists. Applicability of these findings is limited due to the small sample size, inadequate characterization of candidate children, and that specialist pediatric craniofacial surgeons performed these surgeries at an urban tertiary care center. "Usual sites" where ankyloglossia is

diagnosed and treated would have a difficult time extrapolating these findings considering the limitations.

Similarly, the cohort studies were performed solely in urban tertiary care centers. One assessed outcomes on 3-year old children treated for ankyloglossia as neonates compared to those who had untreated ankyloglossia, and a control group without a history of ankyloglossia.[24] Pediatric otolaryngologists made the diagnosis using standardized diagnostic criteria. The reason that infants presented for treatment of ankyloglossia was not identified. Further limiting the applicability is that these patients were all cared for at a tertiary care facility and outcomes were assessed using a non-validated parent reported telephone survey. Thus, there was no objective evaluation of speech. Parents of children with ankyloglossia would have a higher index of concern for speech issues than those whose children never had been diagnosed with tongue mobility restriction. The second poor quality retrospective cohort with a relatively small sample size (n=23) of children a mean of roughly 6 years of age that were similarly divided into those with treated ankyloglossia, untreated ankyloglossia, and a control group.[26] It was performed at a tertiary care facility in an Israeli urban center. Unfortunately, its applicability is limited similarly to that previously described except that speech language pathologists objectively assessed speech using a standardized assessment tool. Both retrospective studies lacked explanations about the rationale for initial surgical intervention or reason parent chose not to intervene.

Applicability of Studies with Social Outcomes

The population studied in the question of benefit of ankyloglossia repair for social concerns included children and adults with wide variation in ages. Studies were rated as poor quality, were retrospective, and few in number. Outcomes in one were assessed by parental report and subject to recall bias[24] and social outcomes assessed were limited to licking lips, cleaning teeth with tongue and eating ice cream. Thus, the social concerns or implications of these issues are unclear. No other comparative study considered social concerns. In addition, at least two case series did consider the impact of ankyloglossia on kissing and playing a wind instrument[42]and drooling and oral hygiene.[33] Limiting these findings was the absence of pre-procedure status of these patients in these domains and how each was assessed. In addition to not including a comparison group of any type, case series are strongly affected by selection bias and are, by nature, not comparative studies. Moreover, patients were selected either by retrospective chart review or as they presented to otolaryngology clinics. Only surgical interventions were studied and no two studies measured the same outcomes. Typically, social concerns were measured as a secondary outcome. The setting was typically the outpatient setting, within academic medical centers.

Implications for Clinical and Policy Decisionmaking

A small body of evidence suggests that frenotomy may be associated with mother-reported improvements in breastfeeding and possibly reduction in nipple pain, when feeding difficulties are present. At this point, the evidence is fairly inconclusive on effectiveness for most outcomes. However, there does seem to be stronger evidence that harms or minimal to none, Thus, given the mixed evidence, clinicians and families will likely need to make individual decisions about pursuing intervention for ankyloglossia-related feeding and speech impediments. Importantly, no research evidence exists to assess any non-surgical interventions, so clinical and policy decisionmaking will necessarily occur in the absence of evidence for nonsurgical interventions

Limitations of the Comparative Effectiveness Review Process

This review included only studies published in English. However, our scan and review of non-English references revealed that high percentage of non-eligible items. Specifically, we determined that of 520 non-English references identified in MEDLINE (search conducted in February 2014), 502 would be clearly excluded based on our criteria. Of the 18 potential includes, six appeared, from the information in the abstract and/or title to be eligible for inclusion; 12 did not include abstracts or sufficient information from the title to make an inclusion decision. Two of these appeared to be case reports and neither gave clear indications on whether harms of interventions were addressed. Given the high percentage of non-eligible items in this scan (97%), we feel that excluding non-English studies did not introduce significant bias into the review.

While we focused the review on comparative studies (studies including an intervention and a comparison group), we provide summaries of case series data to supplement the comparative findings given the small number of studies addressing ankyloglossia interventions. We further specifically sought case reports of any harms associated with ankyloglossia intervention. This approach may provide particularly useful information about harms as we found little evidence of serious harm of surgical interventions, though harms reporting was limited.

Limitations of the Evidence Base

Overall, the evidence base consists of a few small studies that use varied outcomes and provide little information to adequately characterize participants. Infants vary in age at treatment from 6 to 33 days and in reasons for presentation. Studies are focused on neonates and infants who present because of breastfeeding difficulties, and while improving breastfeeding success is an important goal, by definition, this means data are unavailable on infants with ankyloglossia but without feeding difficulties in infancy. The degree to which these infants are likely to go on to develop either feeding, speech or social impediments is inadequately understood. No study effectively assessed mid- and long-term outcomes of frenotomy making it impossible to predict whether mother-reported improvements early in infancy led to longer term breastfeeding.

Finally, we found no comparative effectiveness data on nonsurgical interventions, although they are in use in clinical care, and in surgical studies, case series predominated, providing little comparative data.

Research Gaps

Breastfeeding Outcomes

Future studies should consider direct comparisons of alternative treatments as currently available literature only addressed the comparison of frenotomy to sham. In order to conduct these studies, it would be helpful if the field could agree upon on standardized approach to identifying and classifying ankyloglossia; this would also improve our ability to synthesize the data across studies.

A critical unknown at this point is a good description of the natural history of ankyloglossia by severity, including long term risk of feeding, social and speech impediment. Studies should also consistently report measures of severity.

Given variation in outcomes that may be associated with earlier versus later frenotomy, future studies should assess timing of frenotomy to determine whether more significant reduction in maternal pain is achievable by earlier treatment and whether mothers are more apt to breastfeed longer if done earlier.

A final gap in research is in understanding the durability of outcomes. Good quality comparative studies evaluated breastfeeding effectiveness immediately[7, 20] or within 5 days of frenotomy.[8] However, none adequately assessed whether effectiveness and other outcomes (e.g., changes in maternal nipple pain) were maintained months or, if appropriate, years later. Longer term follow up of both treated infants and controls is needed.

Other Feeding Outcomes

Because there is so little available data on other feeding outcomes, this entire research question represents a gap and a potential area for future research.

Speech and Other Outcomes

Similarly, substantially more research is needed to consider whether treatment of ankyloglossia in infancy prevents future speech impediment as well as whether treatment later in life with frenotomy leads to improvement when speech problems arise. To conduct this research effectively, methods for evaluating risk and presence of speech impediment will need to be standardized, and outcomes agreed upon. Understanding of the natural history of speech concerns in children with ankyloglossia is lacking as are comparative studies that utilize standardized measurement tools for speech outcomes.

Social Concerns Related to Tongue Mobility

No standard definitions of tongue mobility or established norms for mobility exist, and further research is needed to determine such parameters. Social concerns are difficult to measure objectively so there will likely always be a subjective component to social outcomes. Larger studies that assess both treated and untreated individuals could provide useful data to minimize the potential bias found in the existing literature. Similarly, future research in objective measurement tools, or validated self-report tools, is needed.

Harms Reporting

Few studies prespecified harms or provided details of harms collection. Minor, limited bleeding and need for re-operation were reported in some studies, but methods for collecting harms in studies overall were poorly reported. Future studies would benefit from explicit description of methods for harms collection, including estimating blood loss, and assessment and explicit reporting.

Conclusions

A small body of evidence suggests that frenotomy may be associated with improvements in breastfeeding as reported by mothers, and potentially in nipple pain, but with small studies, inconsistently conducted, strength of the evidence is generally low to insufficient. Research is lacking on nonsurgical interventions as well as on outcomes other than breastfeeding, particularly speech and dental outcomes. Harms are minimal and rare; the most commonly

reported harm is self-limited bleeding. Future research is needed on a range of issues, including prevalence and incidence of ankyloglossia and problems with the condition. The field is currently challenged by a lack of standardized approaches to assessing and studying the problems of infants with ankyloglossia.

References

1. Lalakea ML, Messner AH. Ankyloglossia: does it matter? Pediatr Clin North Am. 2003 Apr;50(2):381-97. PMID: 12809329.
2. Suter VG, Bornstein MM. Ankyloglossia: facts and myths in diagnosis and treatment. J Periodontol. 2009 Aug;80(8):1204-19. PMID: 19656020.
3. Hong P, Lago D, Seargeant J, et al. Defining ankyloglossia: a case series of anterior and posterior tongue ties. Int J Pediatr Otorhinolaryngol. 2010 Sep;74(9):1003-6. PMID: 20557951.
4. Messner AH, Lalakea ML. Ankyloglossia: controversies in management. Int J Pediatr Otorhinolaryngol. 2000 Aug 31;54(2-3):123-31. PMID: 10967382.
5. Webb AN, Hao W, Hong P. The effect of tongue-tie division on breastfeeding and speech articulation: a systematic review. Int J Pediatr Otorhinolaryngol. 2013 May;77(5):635-46. PMID: 23537928.
6. Fiorotti RC, Bertolini MM, Nicola JH, et al. Early lingual frenectomy assisted by CO2 laser helps prevention and treatment of functional alterations caused by ankyloglossia. Int J Orofacial Myology. 2004 Nov;30:64-71. PMID: 15832863.
7. Buryk M, Bloom D, Shope T. Efficacy of neonatal release of ankyloglossia: a randomized trial. Pediatrics. 2011 Aug;128(2):280-8. PMID: 21768318.
8. Emond A, Ingram J, Johnson D, et al. Randomised controlled trial of early frenotomy in breastfed infants with mild-moderate tongue-tie. Arch Dis Child Fetal Neonatal Ed. 2013 Nov 18;99(3):F189-95. PMID: 24249695.
9. Baghurst P, Pincombe J, Peat B, et al. Breast feeding self-efficacy and other determinants of the duration of breast feeding in a cohort of first-time mothers in Adelaide, Australia. Midwifery. 2007 Dec;23(4):382-91. PMID: 17126967.
10. Pollard D, Guill M. The relationship between baseline self-efficacy and breastfeeding duration. Southern Online Journal of Nursing Research. 2009;9(4):8p. PMID: 2010524117.
11. Matthews MK. Developing an instrument to assess infant breastfeeding behaviour in the early neonatal period. Midwifery. 1988 Dec;4(4):154-65. PMID: 3210979.
12. Jensen D, Wallace S, Kelsay P. LATCH: a breastfeeding charting system and documentation tool. J Obstet Gynecol Neonatal Nurs. 1994 Jan;23(1):27-32. PMID: 8176525.
13. Methods Guide for Effectiveness and Comparative Effectiveness Reviews. Rockville, MD: Agency for Healthcare Research and Quality. January 2014. Available from: www.effectivehealthcare.ahrq.gov/ehc/products/60/318/CER-Methods-guide-140109.pdf. Accessed May 8, 2014.
14. Agency for Healthcare Research and Quality. Effective Health Care Program. Rockville, MD: Agency for Healthcare Research and Quality. June 2014. Available from: http://www.effectivehealthcare.ahrq.gov/ehc/products/558/1931/Ankyloglossia-protocol-140630.pdf. Accessed May 8, 2014.

15. Eunice Kennedy Shriver National Institute of Child Health and Human Development, National Institutes of Health (NIH), Department of Health & Human Services (DHHS). Preterm Labor and Birth: Condition Information [Internet]. Bethesda, MD: National Institute of Child Health and Human Development, National Institutes of Health, 2014. Available from: http://www.nichd.nih.gov/health/topics/preterm/conditioninfo/Pages/default.aspx. Accessed May 8, 2014.

16. Higgins JPT, Green S. Cochrane Handbook for Systematic Reviews of Interventions The Cochrane Collaboration, 2011. Available from: http://www.cochrane-handbook.org. Accessed May 8, 2014.

17. Viswanathan M, Berkman ND, Dryden DM. Assessing Risk of Bias and Confounding in Observational Studies of Interventions or Exposures: Further Development of the RTI Item Bank [Internet]. Rockville, MD: Agency for Healthcare Research and Quality, 2013. Available from: http://www.ncbi.nlm.nih.gov/books/NBK154461/. Accessed May 8, 2014.

18. Santaguida P, Raina P. McMaster Quality Assessment Scale of Harms (McHarm) for primary studies: Manual for use of the McHarm. [Hamilton, ON: McMaster University, n.d.]

19. Berkman ND, Lohr KN, Ansari M, et al. Grading the Strength of a Body of Evidence When Assessing Health Care Interventions for the Effective Health Care Program of the Agency for Healthcare Research and Quality: An Update. Methods Guide for Effectiveness and Comparative Effectiveness Reviews. AHRQ Publication NO. 13(14)-EHC130-EF. Rockville, MD: Agency for Healthcare Research and Quality. November 2013.

20. Berry J, Griffiths M, Westcott C. A double-blind, randomized, controlled trial of tongue-tie division and its immediate effect on breastfeeding. Breastfeed Med. 2012 Jun;7(3):189-93. PMID: 21999476.

21. Dollberg S, Botzer E, Grunis E, et al. Immediate nipple pain relief after frenotomy in breast-fed infants with ankyloglossia: a randomized, prospective study. J Pediatr Surg. 2006 Sep;41(9):1598-600. PMID: 16952598.

22. Heller J, Gabbay J, O'Hara C, et al. Improved ankyloglossia correction with four-flap Z-frenuloplasty. Ann Plast Surg. 2005 Jun;54(6):623-8. PMID: 15900148.

23. Hogan M, Westcott C, Griffiths M. Randomized, controlled trial of division of tongue-tie in infants with feeding problems. J Paediatr Child Health. 2005 May-Jun;41(5-6):246-50. PMID: 15953322.

24. Walls A, Pierce M, Wang H, et al. Parental perception of speech and tongue mobility in three-year olds after neonatal frenotomy. Int J Pediatr Otorhinolaryngol. 2014 Jan;78(1):128-31. PMID: 24315215.

25. Steehler MW, Steehler MK, Harley EH. A retrospective review of frenotomy in neonates and infants with feeding difficulties. Int J Pediatr Otorhinolaryngol. 2012 Sep;76(9):1236-40. PMID: 22704670.

26. Dollberg S, Manor Y, Makai E, et al. Evaluation of speech intelligibility in children with tongue-tie. Acta Paediatr. 2011 Sep;100(9):e125-7. PMID: 21401716.

27. Srinivasan A, Dobrich C, Mitnick H, et al. Ankyloglossia in breastfeeding infants: the effect of frenotomy on maternal nipple pain and latch. Breastfeed Med. 2006 Winter;1(4):216-24. PMID: 17661602.

28. Blenkinsop A. A measure of success: audit of frenulotomy for infant feeding: problems associated with tongue-tie. MIDIRS Midwifery Digest. 2003;13(3):389-92.

29. Ridgers I, McCombe K, McCombe A. A tongue-tie clinic and service. Br J Midwifery. 2009;17(4):230-3.

30. Edmunds JE, Fulbrook P, Miles S. Understanding the experiences of mothers who are breastfeeding an infant with tongue-tie: a phenomenological study. J Hum Lact. 2013;29(2):190-5. PMID: 23515085.

31. O'Callahan C, Macary S, Clemente S. The effects of office-based frenotomy for anterior and posterior ankyloglossia on breastfeeding. Int J Pediatr Otorhinolaryngol. 2013 May;77(5):827-32. PMID: 23523198.

32. Sethi N, Smith D, Kortequee S, et al. Benefits of frenulotomy in infants with ankyloglossia. Int J Pediatr Otorhinolaryngol. 2013 May;77(5):762-5. PMID: 23453795.

33. Marchesan IQ, Martinelli RL, Gusmao RJ. Lingual frenulum: changes after frenectomy. J Soc Bras Fonoaudiol. 2012;24(4):409-12. PMID: 23306695.

34. Choi YS, Lim JS, Han KT, et al. Ankyloglossia correction: Z-plasty combined with genioglossus myotomy. J Craniofac Surg. 2011 Nov;22(6):2238-40. PMID: 22134257.

35. Miranda BH, Milroy CJ. A quick snip - A study of the impact of outpatient tongue tie release on neonatal growth and breastfeeding. J Plast Reconstr Aesthet Surg. 2010 Sep;63(9):e683-5. PMID: 20493791.

36. Khoo AK, Dabbas N, Sudhakaran N, et al. Nipple pain at presentation predicts success of tongue-tie division for breastfeeding problems. Eur J Pediatr Surg. 2009 Dec;19(6):370-3. PMID: 19750457.

37. Yeh ML. Outpatient division of tongue-tie without anesthesia in infants and children. World J Pediatr. 2008 May;4(2):106-8. PMID: 18661764.

38. Geddes DT, Langton DB, Gollow I, et al. Frenulotomy for breastfeeding infants with ankyloglossia: effect on milk removal and sucking mechanism as imaged by ultrasound. Pediatrics. 2008 Jul;122(1):e188-94. PMID: 18573859.

39. Wallace H, Clarke S. Tongue tie division in infants with breast feeding difficulties. Int J Pediatr Otorhinolaryngol. 2006 Jul;70(7):1257-61. PMID: 16527363.

40. Amir LH, James JP, Beatty J. Review of tongue-tie release at a tertiary maternity hospital. J Paediatr Child Health. 2005 May-Jun;41(5-6):243-5. PMID: 15953321.

41. Griffiths DM. Do tongue ties affect breastfeeding? J Hum Lact. 2004 Nov;20(4):409-14. PMID: 15479660.

42. Lalakea ML, Messner AH. Ankyloglossia: the adolescent and adult perspective. Otolaryngol Head Neck Surg. 2003 May;128(5):746-52. PMID: 12748571.

43. Messner AH, Lalakea ML. The effect of ankyloglossia on speech in children. Otolaryngol Head Neck Surg. 2002 Dec;127(6):539-45. PMID: 12501105.

44. Ballard JL, Auer CE, Khoury JC. Ankyloglossia: assessment, incidence, and effect of frenuloplasty on the breastfeeding dyad. Pediatrics. 2002 Nov;110(5):e63. PMID: 12415069.

45. Masaitis NS, Kaempf JW. Developing a frenotomy policy at one medical center: a case study approach. J Hum Lact. 1996 Sep;12(3):229-32. PMID: 9025430.

46. Godley FA. Frenuloplasty with a buccal mucosal graft. Laryngoscope. 1994 Mar;104(3 Pt 1):378-81. PMID: 8127197.

47. Dave J, Sinha V, Barot D, et al. Speech disorders encountered in routine ENT practice and the role of speech therapy in its effective management. Indian Journal of Otology. 2013 October-December;19(4):169-72. PMID: 2014054877.

48. Klockars T, Pitkaranta A. Pediatric tongue-tie division: indications, techniques and patient satisfaction. Int J Pediatr Otorhinolaryngol. 2009 Oct;73(10):1399-401. PMID: 19660817.

49. Mettias B, O'Brien R, Abo Khatwa MM, et al. Division of tongue tie as an outpatient procedure. Technique, efficacy and safety. Int J Pediatr Otorhinolaryngol. 2013 Apr;77(4):550-2. PMID: 23411135.

50. Argiris K, Vasani S, Wong G, et al. Audit of tongue-tie division in neonates with breastfeeding difficulties: how we do it. Clin Otolaryngol. 2011 Jun;36(3):256-60. PMID: 21752209.

51. Puthussery FJ, Shekar K, Gulati A, et al. Use of carbon dioxide laser in lingual frenectomy. Br J Oral Maxillofac Surg. 2011 Oct;49(7):580-1. PMID: 20728254.

52. Dollberg S, Marom R, Botzer E. Lingual frenotomy for breastfeeding difficulties: a prospective follow-up study. Breastfeed Med. 2014 Jun 3:286-9. PMID: 24892968.

53. Sirinoglu H, Certel F, Akgun I. Subacute massive edema of the submandibular region after frenuloplasty. J Craniofac Surg. 2013 Jan;24(1):e74. PMID: 23348346.

54. Santos Tde S, Filho PR, Piva MR, et al. Mucocele of the glands of Blandin-Nuhn after lingual frenectomy. J Craniofac Surg. 2012 Nov;23(6):e657-8. PMID: 23172517.

55. Opara PI, Gabriel-Job N, Opara KO. Neonates presenting with severe complications of frenotomy: a case series. J Med Case Rep. 2012;6(1):77. PMID: 22394653.

56. Tuli A, Singh A. Monopolar diathermy used for correction of ankyloglossia. J Indian Soc Pedod Prev Dent. 2010 Apr-Jun;28(2):130-3. PMID: 20660983.

57. Lin HW, O'Neill A, Rahbar R, et al. Ludwig's angina following frenuloplasty in an adolescent. Int J Pediatr Otorhinolaryngol. 2009 Sep;73(9):1313-5. PMID: 19560216.

58. Chu MW, Bloom DC. Posterior ankyloglossia: a case report. Int J Pediatr Otorhinolaryngol. 2009 Jun;73(6):881-3. PMID: 19303646.

59. Cunha RF, Silva JZ, Faria MD. Clinical approach of ankyloglossia in babies: report of two cases. J Clin Pediatr Dent. 2008 Summer;32(4):277-81. PMID: 18767457.

60. Nicholson WL. Tongue-tie (ankyloglossia) associated with breastfeeding problems. J Hum Lact. 1991 Jun;7(2):82-4. PMID: 2036160.

61. Fleiss PM, Burger M, Ramkumar H, et al. Ankyloglossia: a cause of breastfeeding problems? J Hum Lact. 1990 Sep;6(3):128-9. PMID: 2400560.

62. Berg KL. Two cases of tongue-tie and breastfeeding. J Hum Lact. 1990 Sep;6(3):124-6. PMID: 2400558.

63. Huggins K. Ankyloglossia--one lactation consultant's personal experience. J Hum Lact. 1990 Sep;6(3):123-4. PMID: 2400557.

64. Mathewson R, Siegel M, D. M. Ankyloglossia: a review of the literature and a case report. J Dent Child. 1966;33:238-43.

65. Good ME. Breastfeeding and the short frenulum. J Human Lact. 1987;3:154-56.

66. Isaiah A, Pereira KD. Infected sublingual hematoma: a rare complication of frenulectomy. Ear Nose Throat J. 2013 Jul;92(7):296-7. PMID: 23904303.

67. Corylllos E, Genna CW, A. S. Congenital tongue-tie and its impact on breastfeeding. American Academy of Pediatrics Section on Breastfeeding Newsletter. 2004;Summer 2004:1-6.

68. Rosin D, Yakir P, editors. Articulation and Naming Test. The International Perspective on Speech Articulation. American Speech-Lanaguage-hearing Association Convention; November 2005; San Diego, CA.

69. Tylor DA. The Effect of Frenotomy in Ankyloglossia on Feeding and Speech in Children [Dissertation]: Liverpool, UK: University of Liverpool, June 2013.

70. Segal LM, Stephenson R, Dawes M, et al. Prevalence, diagnosis, and treatment of ankyloglossia: methodologic review. Can Fam Physician. 2007 Jun;53(6):1027-33. PMID: 17872781.

Abbreviations and Acronyms

AAP: American Academy of Pediatrics
AAPD: American Academy of Pediatric Dentistry
AAO: American Association of Orthodontists
AAO-HNS: American Academy of Otolaryngology – Head and Neck Surgery
ABM: Academy of Breastfeeding Medicine
AF: Analytic framework
AHRQ: Agency for Healthcare Research and Quality
AOS: American Orthodontic Society
ASHA: American Speech-Language-Hearing Association
BSES: Breastfeeding Self-Efficacy Scale
BSES-SF: Breastfeeding Self-Efficacy Scale Short Form
CAM: Complementary and alternative medicine
CER: Comparative Effectiveness Review
CINAHL: Cumulative Index of Nursing and Allied Health Literature
CLCWA: College of Lactation Consultants of Western Australia
CPS: Canadian Paediatric Society
ENT: Ear, Nose & Throat
EMBASE: Excerpta Medica Database
EPC: Evidence-based Practice Center
HATLFF: Hazelbaker Assessment Tool of Lingual Frenulum Function
IBFAT: Infant Breastfeeding Assessment Tool
ILCA: International Lactation Consultant Association
IQR: Interquartile range
KI: Key Informant
KQ: Key Question
LATCH: Latch, Audible swallowing, Type of nipple, Comfort, Hold
LCANZ: Lactation Consultants of Australia and New Zealand
MPQ-SF: Montreal Pain Questionnaire
NHS: National Health Service
MeSH: Medical Subject Headings
NICU: Neonatal intensive care unit
PAS: Pediatric Academic Societies
PICOTS: Population, Intervention, Comparator, Outcomes, Timing, Setting
PQDT: ProQuest Dissertations & Theses
RCT: Randomized controlled trial
SF-MQP: Short Form McGill Pain Questionnaire
SRDR: Systematic Review Data Repository
TEP: Technical Expert Panel
VAS: Visual Analog Scale for Pain